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IS-01

One year in review

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Fibromyalgia is a complex disease that until recently lacked specific diagnostic criteria for clinical use. The establishment of new diagnostic criteria has allowed for more accurate diagnoses of the condition. A recent observational study of 200 fibromyalgia patients identified physical findings that clinicians should consider when diagnosing the disease (1). In addition, several measurements have been proposed as altered in fibromyalgia patients, including physical measurements, autonomic nervous system function, serologic features, and imaging results. Physical measurements showed that individuals with fibromyalgia walked slower, had shorter strides and lower cadence, had decreased muscle function and cervical extensor muscle thickness (2), and had longer reaction times. Fibromyalgia sufferers have an impaired autonomic cardiovascular response (3). Studies also suggest that characteristic serologic features and imaging techniques could aid in the diagnosis of fibromyalgia (4, 5). Increased sensitivity to pressure, alterations in cranial nerves, and alterations in gait, among other physical findings, provide significant credibility to the disease and suggest that clinicians should be aware of them in addition to the diagnostic criteria. By utilizing these measurements and diagnostic criteria, clinicians can more accurately diagnose and treat fibromyalgia patients.

The differential diagnosis of non-localized musculoskeletal pain is a vast and complex area that requires a systematic multidisciplinary approach. FM often accompanies other rheumatic diseases such as connective tissue disorders, ankylosing spondylitis, and spondyloarthritis. A systematic multidisciplinary approach is required, with many patients requiring referral to specialties such as rheumatology or endocrinology. A recent review aimed to comprehensively examine the clinical presentation of various causes of generalized musculoskeletal pain and create a mental framework to aid diagnostics; the authors suggested that a systematic multidisciplinary approach is required for the differential diagnosis of non-localized musculoskeletal pain (6).

Juvenile Fibromyalgia (JFM) is a chronic condition that affects adolescents and is characterized by chronic widespread pain (CWP). Studies have found that around 3.19% of children/adolescents have CWP (7), with risk factors including mental health, neurological, genitourinary, gastrointestinal, and throat problems. However, there are currently no diagnostic criteria for fibromyalgia in children, leading to subspecialty referrals and extensive imaging and testing. JFM patients show similar characteristics to individuals suffering from chronic pain caused by headache or joint pain in terms of depression, anxiety, somatization, and medication use, but with higher prevalence among women and sleep disturbances. Distinguishing between JFM and small fiber neuropathy (SFN) is important, as recommended therapies differ, but more studies are needed in this direction (8-10).

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IS-02

What's new with chronic fatigue? Insights into mechanisms of fatigue in a post-COVID era

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Chronic fatigue is a prevalent and debilitating condition that affects a significant portion of the population. Despite much research, the underlying mechanisms of fatigue are still not fully understood (1). The COVID-19 pandemic has brought new attention to this issue, highlighting the need for further investigation into the causes and mechanisms of fatigue in the post-COVID era.

Recent research on chronic fatigue focused on the biological and psychosocial factors that contribute to the development and persistence of fatigue, including the impact of inflammation, neuroinflammation and oxidative stress (2). In this regard, the potential long-term effects of the COVID-19 pandemic opened a whole new chapter on research on fatigue, including the immunological consequences (3) and the psychological impact of social distancing and isolation. Furthermore, the key role of sleep has been recently underlined, due to its indispensable role for neuroendocrine balance (4). To address the complex nature of chronic fatigue, interdisciplinary collaboration is crucial. This includes collaboration between researchers, clinicians, and patients, to develop a comprehensive understanding of the mechanisms behind fatigue and pain to develop effective strategies for its prevention and treatment (5-8).

In conclusion, research focusing on fatigue has to include not only addressing the biological and psychosocial factors underlying fatigue, but also considering the impact of larger social and cultural factors, such as the COVID-19 pandemic. With a multidisciplinary approach and continued research, we can hope to make significant progress in understanding and treating chronic fatigue in the post-COVID era.

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IS-03

Keynote Lecture: Overview of nociplastic pain and central sensitization

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The term nociplastic pain is the third mechanistic descriptor, in addition to nociceptive and neuropathic pain. It was adapted in 2017 by the International Association for the Study of Pain (IASP). Nociplastic pain is defined as “pain that arises from altered nociception” that cannot be fully explained by nociceptive or neuropathic pain mechanisms (1). It is intended for patients presenting with pain and hypersensitivity with clinical and psychophysical findings that suggest altered nociceptive function. Typical such conditions are fibromyalgia (FM), chronic regional pain syndrome (CRPS) type 1, certain so called chronic non-specific neck- and back pain conditions and visceral disorders such as irritable bowel syndrome and bladder pain syndrome (1). The IASP Terminology Task force has published classification criteria and a grading system for nociplastic pain affecting the musculoskeletal system (2). To classify pain as nociplastic a minimum of 4 conditions need to be fulfilled: 1) pain duration >3 months, 2) a regional, multifocal or widespread rather than discrete distribution of pain, 3) the pain cannot entirely be explained by nociceptive or neuropathic mechanisms, and 4) clinical signs of pain hypersensitivity are present in the region of pain (2). Pain that cannot be classified as either nociceptive, neuropathic or nociplastic is referred to as pain of unknown origin, or non-classifiable pain. Thus, nociplastic pain is NOT a new term for pain of unknown origin (2). The terminology harmonizes with the International Classification of Diseases (ICD-11) where nociplastic pain conditions are classified as “chronic primary pain”, highlighting the concept of pain as a disease (2, 3). In contrast, nociceptive and neuropathic pain conditions are classified as “secondary pain”, where the pain is a symptom (3).

Central sensitization is a neurophysiological term defined by IASP as “an increased responsiveness of nociceptive neurons to their normal input and/or recruitment of a response to normally subthreshold inputs”. In central sensitization, this pertains to central nociceptive neurons and encompasses increased responsiveness due to dysfunction of endogenous pain modulatory mechanisms. Central sensitization can be caused by bottom-up mechanisms, i.e., activity in primary nociceptive afferents sensitizes central neurons and/or top-down mechanisms, namely increased descending facilitation or decreased descending inhibition of pain signalling. Clinically, sensitization may be inferred indirectly from phenomena such as hyperalgesia or allodynia, in which case it is impossible to distinguish peripheral from central sensitization. However, an inability to activate descending pain inhibitory mechanisms has been documented in nociplastic pain, e.g. FM (4, 5) and can be interpreted as central sensitization. In addition, FM patients also present with aberrant cortical pain processing related to pain expectations and catastrophizing (6, 7). Central sensitization is a physiological term and thus not synonymous with the pain classifier “nociplastic pain”. However, although sensitization is not specific for any pain type, be it nociceptive, neuropathic, or nociplastic, sensitization still remains a hallmark of nociplastic pain conditions (1, 2, 8).

On a more controversial note, there are indications that not only central, but also peripheral sensitization can be important in FM. Recent evidence suggests that the pain in a subgroup of FM patients (approx. 50%) may be driven by autoreactive antibodies binding to satellite glia cells (SGC) in the dorsal root ganglia, and causing activation and sensitization of primary nociceptive afferents (9). In support of this, a positive association between the levels of these SGC binding antibodies in individual patients and their pain intensity was found in two different cohorts, one Swedish and one Canadian (10). This pain cannot be classified as neuropathic since there is no known primary disease or lesion of the somatosensory nervous system, nor can it be classified as nociceptive as there is no identified mechanism that would activate high-threshold *sensory receptors* of the peripheral somatosensory nervous system. Given that these patients have chronic, widespread pain and present with pain hypersensitivity, the pain fulfills the criteria of nociplastic pain, i.e. altered nociception not explained by neuropathic or nociceptive mechanisms.

In conclusion, nociplastic pain should not be confused with central sensitization, nor with pain of unknown origin. In addition to nociceptive and neuropathic pain, nociplastic pain is a third mechanistic pain descriptor with a clear definition (1), and for nociplastic pain manifesting in the musculo-

skeletal system also clinical criteria and grading system (2). The term “nociplastic pain” has the potential to facilitate communication and validate the patient’s pain experience. It aids clinicians to explain to their patients that the nociplastic pain is a disease in its own right and not a symptom of underlying peripheral pathology yet to be identified (with additional examinations). Finally, classifying nociplastic pain is important for correct choice of treatments e.g. drugs (mainly centrally acting and not opioids) (1, 2).

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IS-04

Cytokines and miRNA in chronic pain

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Strong inflammatory components emerging for many chronic pain disorders. In particular, interleukin 6 (IL-6) is a very important regulator of pain pathogenesis along the pain pathway. It has pleiotropic effects which in most tissues are mediated by IL-6 binding to its soluble alpha-receptor subunit and membrane bound IL-6 signal transducer gp130 which is ubiquitously expressed in virtually all tissues and cell types. In addition, GM-CSF, Interleukin 1 (IL-1 β) and TNF- α are important pro-algesic cytokines which have received major attention by preclinical and clinical pain research. Mechanistically, these cytokines via specific membrane receptor complexes sensitize primary nociceptive afferents to thermal and mechanical stimuli and affect synaptic transmission as well as microglia functions along the entire pain pathway in the central nervous systems. The classical proinflammatory mediators not only regulate neuroimmune processes but they also can affect the expression of non-coding RNA (ncRNA) species which are emerging as novel hub regulators of both neuronal and immune functions. Recently, ncRNAs are emerging as novel molecule species offering promising new applications for clinical use both for diagnosis based on signatures of differential expression and treatments for manipulating them in relevant tissues. Among the different types of ncRNAs, microRNAs (miRNAs) have been most extensively investigated. miRNAs are small ~22 nucleotide long RNA sequences and regulate gene expression by inducing either translational repression or degradation of targeted mRNAs depending on the degree of sequence complementarity. As miRNAs can simultaneously target entire clusters of target genes, they act as regulatory hubs and efficiently control entire signaling pathways affecting neuron and immune cell function as well as neuroimmune communication. Specific miRNAs have been associated with changes of nociceptor thresholds for mechanical and thermal stimuli, the development of hyperalgesia and allodynia, and the chronification of pain states in both animal models and human pain related disorders. Although the consistency of reports regarding pro- versus analgesic roles of specific miRNA families to date are not fully consistent, miRNA related mechanisms offering novel therapeutic strategies for pain disorders. In contrast, the availability of anti-inflammatory therapies neutralizing specific cytokines and their receptors is well advanced mainly in the rheumatology and immunology fields and respective therapies are on the market for the treatment of immunological and other disorders. Thus, cytokine neutralizing biologics offer opportunities for repurposing towards fast-track applications for the benefit of patients suffering from pain disorders.

IS-05

Fibromyalgia: Imbalance of Threat and Soothing Systems (FITSS)

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FITSS (Fibromyalgia Imbalance of Threat and Soothing Systems) (1) is a model of fibromyalgia (FM) that attempts to integrate the myriad mechanisms involved in this disease, with emphasis on psychosocial and neurophysiological observations, under a common framework based on the salience network.

The model sits on three pillars: the stressed psychosocial milieu that predominates in FM, which provides a persistent source of threat signals, the scarcity of positive affect that is typical of this condition, reflecting low levels of soothing/safeness and the Brain's Salience Network, which is kept in persistent alarm mode by this imbalance between perceived threat and soothing. The Salience Network includes most of the neurological structures that have been, so far, associated with FM. In fact, the neural regulation of pain and emotion is tightly woven together, and this opens the opportunity for powerful bidirectional interactions.

This model provides a framework capable of bringing together apparently disparate observations such as the higher prevalence of psychopathology and early childhood adversity as well as gender difference in FM, observed changes in the HPA axis and the autonomous nervous system, visceral manifestations of the disease, heightened activity in the insula and default mode network, among many others. This perspective underlines the commonality between FM and many of its common co-morbidities, such as irritable bowel syndrome, temporomandibular disorder, and post-traumatic stress disorder calling for the exploration of higher-grade mechanisms that may underlie these different phenotypes.

Recent and well supported psychosocial constructs, like Gilbert's Three System Affect Regulation Model (2) and the Generalized Unsafety Theory of Stress (Brosschot *et al.*) (3) are analysed in parallel with the predominant neurophysiological observations in FM, by a diversified group of experts from all these fields.

It is emphasized that the model is not meant to state or infer that psychological stress is the only or even the major trigger or driver of FM in all or even in most patients. Psychological features ought to be seen as just one among a large number of players with powerful mutual influences, generating a large number of relevant vicious circles that maintain the process. FM may emerge in different sites and hubs of this grid and once the nexus is launched it is virtually impossible to clearly separate cause and consequence.

The authors hope that this model will shed new light on existing psychosocial and biological observations, and inspire future research to address the many gaps in our knowledge about fibromyalgia, ultimately stimulating the development of novel therapeutic interventions.

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IS-06

Anti-satellite glia cell antibodies are associated with symptom severity in fibromyalgia

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While it is well recognized that alterations in central pain processes are part of the pathology in fibromyalgia, accumulating evidence show that fibromyalgia is also associated with changes in the peripheral nervous system and the immune system. We have established a link between the adaptive immune system and fibromyalgia symptoms by assessing behavioral and cellular changes in mice after transfer of antibodies (IgG) from fibromyalgia subjects. We found that injection of fibromyalgia patient IgG, but not IgG from healthy controls to mice induces pain-like behaviors in form of increased sensitivity to mechanical and cold stimulation and reduced locomotor activity. After transfer, fibromyalgia IgG accumulate in the dorsal root ganglion (DRG) where they bind to satellite glia cells (SGCs). In the experimental setting, the binding was associated with morphological and transcriptional changes coupled to altered SGCs activity. In addition, IgG from individuals with fibromyalgia show a higher binding intensity to SGCs in human DRG sections compared to IgG from healthy controls. These findings suggest that autoantibodies could be part of fibromyalgia pathology. We examined how frequently fibromyalgia patients have anti-SGC antibodies and how anti-SGC antibodies associate with disease severity. Elevated anti-SGC IgG titers were associated with higher levels of self-reported pain, higher fibromyalgia impact questionnaire scores and increased pressure sensitivity but was not associated with fibromyalgia duration, pain duration, Beck's depression inventory, BMI or age. We clustered the fibromyalgia serum samples based on the severity of the disease and found that the severe fibromyalgia group had elevated anti-SGC IgG compared to the mild fibromyalgia and control groups. This association was also detected in a Canadian fibromyalgia cohort. Furthermore, the severe fibromyalgia group had elevated IgG binding to SGCs in human DRG sections compared to the mild fibromyalgia and control groups. These results suggest that autoantibodies underlie fibromyalgia in a subgroup of patients. Thus, advancing our knowledge on the role of the immune system in fibromyalgia is critical as it could provide a new path to personalized treatment options that target autoantibodies or autoantibody production for symptom relief.

IS-07

Keynote lecture: Genetic and epigenetics of fibromyalgia and chronic pain

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Limited data exist to inform mechanism-based understanding and management of fibromyalgia and other chronic pain conditions, and thus, there is a clear unmet need to better define the molecular mechanisms of chronic pain to develop novel treatment strategies. Generating knowledge regarding the molecular pathophysiology of pain states using human cohorts has an obvious advantage over animal models, and it can be achieved using molecular and cellular genome-wide approaches in human cohorts. Crucially, such approaches are hypothesis-free, and thus both heuristic and resulting in the unbiased interpretation of data, not restricted by or funneled through specific hypotheses or gene candidates. In this lecture, Dr. Diatchenko will discuss the application of such approaches for studying the molecular pathophysiology of chronic pain resulting in the generation of new hypotheses. First, by using genome-wide genome-wide association studies (GWASs) to compare genetic determinants of chronic pain manifested in only single body site in comparison with chronic overlapping pain. This study found that different genetic signals underlie chronic single-site and multisite pain with much stronger genetic contributions for the latter, with the DCC netrin 1 receptor (DCC) as the top gene and axonogenesis as top pathway. Second, by conducting unbiased multiparametric flow cytometry analyses of peripheral blood mononuclear cells from fibromyalgia patients and healthy controls. This analysis, together with other global genetic and transcriptomic pathway analyses, functional *in vitro* cell assays, and analysis of skin biopsies, suggested that chronic activation and redistribution of circulating natural killer cells to the peripheral nerves contribute to the immunopathology associated with fibromyalgia. Third, by applying transcriptome-wide analyses in peripheral immune cells of patients with fibromyalgia, facial pain, and low back pain. These studies, together with *in vitro* cell assays, identified the protective role of transient neutrophil-driven up-regulation of inflammatory responses against the transition from acute to chronic pain. The inability of neutrophils to upregulate proper inflammatory response was associated with low-grade inflammation and chronic pain. Overall, these findings support the critical role of neuroimmune interactions in pain resolution processes that involve, over time, different subsets of immune cells. Thus, the employment of unbiased genome-wide approaches in human cohorts can lead to generating knowledge regarding the molecular pathophysiology of fibromyalgia and other chronic pain conditions.

IS-08

The role of hyperalgesia in chronic widespread painChristopher Sivert Nielsen^{1,2}, Ólöf Anna Steingrimsdóttir³, Audun Stubhaug^{2,4}, Bo Engdahl³¹Department of Chronic Diseases, Norwegian Institute of Public Health, Norway;²Department of Pain Management and Research, Oslo University Hospital, Norway;³Department of Physical Health and Ageing, Division of Mental and Physical Health, Norwegian Institute of Public Health, Norway; ⁴Institute of Clinical Medicine, University of Oslo, Norway

Background. Chronic pain in general, and chronic widespread pain in particular, are associated with increased pain sensitivity. Given identical noxious stimuli patients with these conditions rate pain as more intense and display lower pain thresholds and pain tolerance limits than healthy controls. This finding suggest that increased pain sensitivity may reflect a disposition or risk factor for developing chronic pain, and that experimental pain paradigms could be used to assess risk of new-onset chronic pain and chronic widespread pain. However, while cross-sectional relationships between chronic pain and pain sensitivity have repeatedly been demonstrated, prospective studies have thus far not been published, making this as an interesting, but heretofore unsupported hypothesis.

Methods. In 2007-08 our study group conducted cold-pressor tests of 10,470 participants in the population-based Tromsø Study (Age 30-87, 53% women). Of these, 6,506 participated in follow-up examinations 8 years later in 2015-2016, whereof 4336 were pain free at baseline and could be included

in prospective analysis of new-onset chronic pain. The cold-pressor procedure consisted in the participants submerging their hand in circulating cold (3°C) water, with the instruction to hold it there as long as they were able. Pain tolerance was recorded as time in the water, with a maximum limit of 106s. Both study waves included screening for chronic pain, including pain duration, pain intensity scoring and body sites with pain. Chronic pain was considered present if the reported pain duration was ≥ 3 months and pain intensity was $>3/10$ on a numeric rating scale. If neither criterion was met the number of body sites with pain was set to zero. Similarly, chronic pain intensity was set to zero if the duration of pain was <3 months. We conducted cross-sectional analysis at baseline, and prospective analysis of new onset-pain at follow-up with cold-pressor tolerance at baseline as the predictor and chronic pain intensity (0-10) and number of chronic sites (0-8) as outcomes, using linear and Poisson regression models respectively. All analysis were adjusted for age and sex.

Results. In the cross-sectional analysis both chronic pain intensity (Beta -0.34, $p<0.001$) and number of body sites with pain (IRR 0.92, $p<0.001$) decreased with cold-pressor tolerance time (minutes). Results were similar when considering new onset pain 8 years later, with effect sizes slightly larger for both pain intensity (Beta -0.44, $p<0.001$) and number of body pain sites (IRR 0.89, $p=0.007$).

Conclusions. Our results demonstrate that experimental tolerance is predictive of new-onset chronic pain eight years later. Participants who abort the cold-pressor test early are more likely to experience more intense pain and to develop pain in multiple body sites. While the results do not prove causality, they do give strong indication that the observed association between pain sensitivity and chronic pain is not due to reverse causality.

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IS-09

Insights into the field of sleep

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The objective measures of sleep. Sleep is a natural function under the control of genetic, circadian and homeostatic processes. The objective measurement of sleep is provided by polysomnographic studies which allow identification of sleep stages and cycles. Stages N1 and N2 compose superficial non-REM sleep, stage N3 represents deep non-REM sleep, while stage REM is characterized by rapid eye movements, low voltage electroencephalographic activities, muscle atonia and dream experiences. The succession of stages and cycles (periodic alternation of non-REM and REM stages) defines the macrostructure of sleep. To warrant a flexible and adaptive architecture, the sleeping brain is endowed with windows called arousals, which are involved in the resistance and porosity of the sleep structure. A single arousal has limited impact on sleep continuity and on the individual's health. However, in the texture of physiological sleep, arousals rarely appear as isolated phenomena, while they are often aggregated with other arousals in swarms. Ordered and periodic, sequences of arousals compose the cyclic alternating pattern (CAP). CAP translates a condition of arousal instability, which involves simultaneously motor activity and vegetative functions. The percentage of CAP time over non-REM sleep time quantifies the microstructural sleep parameter called CAP rate. CAP, REM and non-REM stages are fundamental guardians of sleep resilience. Poor sleep and sleep disorders occur when these and other nocturnal sentinels are overcome by internal or external perturbations.

Insomnia. Insomnia is characterized by an inability to initiate or maintain sleep. It may also take the form of early morning awakening or non-restorative sleep. However, nocturnal disturbances are often accompanied by diurnal impairment including, fatigue, poor concentration, reduced attention, mood disorders and sleepiness. In other words, insomnia is a 24-hour disorder which can be classified as an independent entity (chronic insomnia disorder) or as the by-product of other sleep, mental or medical diseases.

Sleep and pain. Painful syndromes are often accompanied by insomnia or poor sleep. Rheumatic pathologies neurological diseases (neuropathic pain, multiple sclerosis, headache), duodenal ulcer, irritable bowel syndrome, cancer pain and dysmenorrhea, are chronic painful conditions that are often associated with a sleep disorder. In turn, insomnia has a negative effect on pain increasing its perception, reducing its tolerance, favoring central sensitization and impairing the effects of descending modulation.

Sleep in fibromyalgia. Patients with fibromyalgia (FM) may show sleep fragmentation and a curtailment of total sleep time. A reduction in stages N3 and REM and an enhancement of CAP are polysomnographic markers of poor sleep quality. Increased autonomic tones of low frequency (sympathetic) associated with lower levels of high frequency (vagal) tone have also been described in FM. Compared to healthy subjects, sleep apneas occur more frequently in FM patients, and patients with FM plus obstructive sleep apnea syndrome are significantly older and complain of poorer sleep. Mediated by dopamine neurotransmission and iron metabolism, restless legs syndrome shows a higher prevalence in patients with FM. Finally, patients with FM often complain of depressive disorders which are closely related to insomnia.

Treatment strategies. Specific therapies are still unavailable to treat both painful syndromes and insomnia. However, since sleep and pain are linked by a bidirectional influence, analgesic agents can improve sleep duration and quality. In turn, any treatment (drugs or cognitive behavioral therapy) which increases sleep resilience can raise the sensitive threshold in painful settings.

IS-10

The evolving role of small fibre neuropathy in fibromyalgia

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The fibromyalgia syndrome is a clinical condition manifesting with widespread pain and multiple symptoms, including fatigue, sleep disorders, cognitive and autonomic disturbances (Häuser and Fitzcharles, 2018).

Previous skin biopsy and microneurographic studies found a reduced intraepidermal nerve fibre density and abnormal C-fibre activity in approximately 50% of patients with fibromyalgia. These findings, which parallel a small-fibre neuropathy, are commonly defined as small-fibre pathology (Grayston *et al.*, 2019).

These findings are in line with recent preclinical investigations, which indicated that dorsal root ganglia damage, due to circulating autoantibodies, may play a role in fibromyalgia (Goebbel *et al.*, 2021).

Although patients with fibromyalgia share similar skin biopsy abnormalities with patients with small-fibre neuropathy, the relationship between small-fibre pathology and the symptoms and signs that patients with fibromyalgia experience is still an issue of controversy. Whereas several studies have reported that patients with fibromyalgia have impaired sensory profiles at the quantitative sensory testing and abnormal nociceptive evoked potentials, other studies showed that small-fibre pathology is not associated with clinically meaningful abnormalities of the somatosensory nervous system (Fasolino *et al.*, 2020).

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IS-11

The transition to chronic pain: risk factors and potential for prevention

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Chronic pain is a highly prevalent condition, estimated to affect between 20–50% of adults globally. Localized musculoskeletal pain and headache are leading categories of chronic pain, while about 10% of patients suffer from widespread pain.

Chronic pain has a significant impact on an individual's quality of life, leading to disability, reduced productivity, and increased healthcare utilization. Furthermore, chronic pain leads to a tremendous burden on society, in terms of healthcare costs and loss of productivity.

Pain is defined chronic when it persists for over 12 months beyond the acute processes of inflammation and healing. The pathophysiology of pain processing encompasses complex sensory, inflammatory, immune, and endocrine interactions at the cerebral, spinal, and peripheral levels. Transition from acute to chronic pain involves a complex interplay of physiological and psychological factors, including genetic factors, peripheral and central sensitization and inflammatory processes. These factors culminate in the instigation of neuroplasticity - the brain's ability to adapt and change in response to experiences, and changes in pain modulation systems responsible for regulating the intensity and duration of pain signals. Poor sleep has considerable reciprocal influence on chronic pain. Psychological factors such as depression, anxiety, pain catastrophizing, perceived injustice and previous pain experience increase the likelihood of transition to chronic pain, and can further exacerbate pain perception making it more difficult to cope with pain. Lack of social support also increases the risk of chronic pain.

Understanding the pathways and risk factors involved in the transition from acute to chronic pain is crucial for developing effective intervention strategies that can prevent and manage chronic pain. Early recognition of patients at high risk for developing chronic pain, and implementation of early multimodal biopsychosocial pain management will help to minimize the development of chronic pain in daily practice.

IS-12

Obesity, bariatric surgery, and chronic pain

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Fibromyalgia (FM) is a syndrome characterized by widespread musculoskeletal pain often associated with sleep disturbances, fatigue, memory complaints, and psychiatric comorbidity, mainly mood and anxiety disorders. It is thought that FM derives from a central sensitization (CS) process characterized by increased responsiveness of nociceptive neurons in the central nervous system to either normal or sub-threshold afferent input. Studies have shown that patients with FM syndrome tend to be overweight and obese, but the impact of a high body mass index (BMI) on clinical severity in patients with FM is still controversial. We have demonstrated that overweight/obese patients with FM are significantly more impaired in all of the symptomatological and functional domains as measured using the revised Fibromyalgia Impact Questionnaire (FIQR), the modified Fibromyalgia Assessment Status (ModFAS) questionnaire, and the Polysymptomatic Distress Scale (PDS) than Underweight/Normal patients, thus suggesting that being obese/overweight has an additional effect on symptoms and function. The relationship between a high BMI and FM are still unclear, but it has been suggested that the reduction in physical activity induced by musculoskeletal pain may lead to a higher BMI, or that a higher BMI causes pain as a result of increased strain on weight-bearing joints. Studies have demonstrated that severely obese individuals candidates for bariatric surgery report musculoskeletal pain both in a single anatomical region and in multiple locations. Observational evidence showed that even if most patients who undergo bariatric surgery experience significant improvement in presurgical pain, some report that surgery could result in new pain issues.

If the joint damage can explain localized pain due to excess weight in areas with an increased mechanical load, such as the ankles, feet, lower back, and knees, the pathogenetic mechanisms underlying multisite musculoskeletal pain are still unclear. Furthermore, patients with FM tend to be overweight and obese and share with severely obese patients seeking bariatric surgery some clinical features, such as disturbed sleep and psychiatric bipolar spectrum comorbidity profile, suggesting common pathogenetic pathways.

IS-13

Sexuality and fibromyalgia. a call for dialogue

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According to the WHO, sexuality is defined as a central aspect of being human throughout life and encompasses sex, gender identities and roles, sexual orientation, eroticism, pleasure, intimacy and reproduction while sexual health is considered a state of physical, emotional, mental and social well-being in relation to sexuality. Therefore, an impaired sexual function negatively impact people's quality of life, directly or indirectly affecting one or more domains of sexual and relationship health. Fibromyalgia (FM) is a chronic disorder characterized by widespread musculoskeletal pain associated with fatigue, sleep and cognitive disorders as well as a wide spectrum of other physical and psychological symptoms. FM worsens patient's quality of life and, by altering their health perception, could also have an impact on patient's sexual function. Studies conducted regarding sexual dysfunction (SD) in FM have mainly examined female sexual dysfunction (FSD) in the context of heterosexual relationships. According to the available literature, more than 85% of female patients diagnosed with FM suffer from SD and a clear association exist between FM and FSD based on the evidence that FM patients often experience decreased sexual desire, arousal, lubrication, orgasm and satisfaction while encounter increased pain during or after sexual activity. Among this wide range of FSD experienced, the most frequent appear to be a decreased sexual desire, both dyadic and autoerotic. It has been demonstrated that a negative correlation exists between sexual desire and disease severity, number of tender points and pain intensity, leading to the conclusion that pain might play a greater role in the development of FSD. Lower pain threshold could also explain the major frequency of pain during intercourse and the increased vaginal tightness reported by FM patients, possibly associated with the development of vulvodynia. Moreover, it has been demonstrated that symptoms of depression and antidepressant medication are associated with lower sexual desire in FM patients showing that depression could be implicated and worsen FSD. It must be highlighted that, although depression and anxiety could co-exist in FM patients, the poor sexual performance is directly due to FM and could not be explained only by the presence of mood disorders. Therefore, it seems reasonable to assume that both physiological - such as widespread pain, fatigue, stiffness or vulvodynia - and psychological factors - in particular depression and anxiety - might be implicated in the quite complex phenomenon of SD but the exact underlying pathophysiological mechanisms remain unclear. When interrogated regarding sexuality, female FM patients answer that it is important for their quality of life and, for the majority of them, it appears as a physical, psychological, emotional and relational need. For these reasons, women require support and understanding from both their partners and health care professionals. In spite of this, studies have shown that discussion regarding sexual health between patients and health care providers are often avoided, mostly because of stigma and embarrassment. It is therefore important for clinicians to be aware of the issue, start the discussion and allow the patients to expose any concerns regarding their sexuality. In conclusion, FM is commonly associated with SD, at least in female heterosexual patients, while literature regarding SD in male patients and different sexual oriented patients is lacking. Future research should undoubtedly evaluate the burden of SD in these groups other than focus on pathophysiological mechanisms underlying the association between FM and SD.

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IS-14

Gut feelings: IBS revisited

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The previous decade has seen significant advances in our understanding of the contribution made by peripheral changes in gut function to the generation of symptoms which collectively lead to the diagnosis of irritable bowel syndrome (IBS). This has prompted the introduction of the term "disorder of gut brain interaction" as a replacement for "functional GI disorder" to address the false perception that IBS is less real and often considered psychiatric or undefined in nature. This presentation will review studies from my group and others which have repeatedly shown the ability of tissue, blood, and faecal samples from IBS patients to modulate endpoints mechanistically relevant to IBS symptomology such the activation of visceral nociceptors responsible for the generation of abdominal pain and visceral hypersensitivity. Consistent with the diagnosis of IBS these effects occur in the absence of marked histological and transcriptomic changes within the gut. However careful study of samples from well phenotyped patients indicates that the development of a pro-nociceptive bowel is a feature of patients that display visceral hypersensitivity. This patient subgroup is treated by antihistamines consistent with the contribution of altered mast cell function to symptom generation in these patients who typically display diarrhoea in addition to abdominal pain. Most recently this has been linked to a localised loss of oral tolerance to food antigens within the bowel of IBS patients, in addition to the activation of TRP channels expressed on visceral nociceptors mediated in part by histamine and the production of endogenous lipids downstream of proteinase signalling. By contrast tissue samples from IBS patients with constipation display a different lipid mediator profile, which we have shown stimulates an alternative subset of visceral nociceptors through the activation of MRGPRD receptors highlighting a possible need for stratified treatments for diarrhoea versus constipation predominant IBS based on their differing mediator profiles and nociceptor populations activated. Finally, we will consider the contribution of intestinal dysbiosis to symptom generation in IBS and the opportunities to treat IBS through dietary modulation and conventional pharmacotherapy.

IS-15

From long COVID to fibromyalgia: insights from an evolving trajectory

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Three years after the outbreak of the COVID-19 pandemic, a broader perspective is developing regarding the long-term consequences of the condition, both on a clinical as well as a patho-physiological basis. While both public attention as well as medical research initially naturally focused on the acute, life-threatening aspects of the infection as well as on the dramatic efforts to develop vaccinations in unprecedented haste, increasing resources are currently being turned towards the more chronic aspects related to the condition. At the same time, COVID-19 appears to be evolving and developing. The ongoing emergence of novel variants is associated on the one hand with increased vaccine-escape and transmissibility. On the other hand, due to emergence of less virulent variants, such as the Omicron lineage, as well as the fact that far more individuals contracting the illness currently have a prior exposure to either vaccines or to the virus (or both), many cases result in a mild clinical course. Nonetheless, long-COVID continues to pose a challenging, incompletely understood syndrome. While a minority of cases manifest serious, organ specific late complications such as pulmonary disease, myocardial dysfunction or thrombosis, most individuals diagnose with long-COVID present with a constellation of symptoms centering around chronic fatigue, cogni-

tive difficulties, and sympathetically driven symptoms such as palpitations and tachycardia. Within this population, some patients recover, while others appear to move on towards a chronic condition. Within this group, a subset of patients acquire symptoms of widespread musculoskeletal pain, which in many cases becomes indistinguishable from classical fibromyalgia.

On a clinical basis, individuals developing fibromyalgia symptoms as part of their course of long COVID may sometimes a history of various pain conditions, possibly indicating a predisposition, although in other cases the viral infection appears to be the sole trigger leading towards the fibromyalgia phenotype. Notably, in this aspect COVID-19 is but the last infectious condition to -date to be added to the list of fibromyalgia triggering agents, as fibromyalgia has often previously been described as being triggered but EBV, Hepatitis, Lyme disease etc.

Current insight into the classification of chronic pain conditions such as fibromyalgia has built upon the concept of nociplastic pain, a novel definition referring to pain that is neither nociceptive or neuropathic but rather attributed to aberrant and increased processing of pain within the nervous system. This type of pain, which is classical of fibromyalgia, is the focus of ongoing research in the field of neuroscience in an attempt to uncover specific pathways and connectivity - patterns associated with nociplastic pain (1). Similar attempts are currently being initiated in studying the neuroscience of long-COVID and these efforts are likely to elucidate both the pathophysiological overlap between fibromyalgia and long-COVID as well as the more unique aspects of the post viral condition (2). At the same time, intriguing evidence has emerged regarding the possibility of persistent viral infection in at least some patients, a finding which raises curiosity about the possibility that some aspects of fibromyalgia might be related to hitherto unsuspected chronic infections. Last but not least, the role played by the autonomic system in both fibromyalgia and long remains a topic of interest. There is little specific research regarding the treatment of long COVID in general and of long COVID-associated fibromyalgia in particular. Notably, many patients suffering from such symptoms are followed by either infectious disease specialists or by other physicians less - acquainted with the multi-dimensional treatment of fibromyalgia, and thus may face challenges regarding the timely diagnosis and treatment of their symptoms.

There is thus a need for ongoing research regarding the overlap between fibromyalgia and long COVID, as well as a need for increased publicity and medical education in order to assure that patients in this clinical situation are given proper treatment. Increasing understanding regarding the various aspects of pain among post-COVID patients, delineating the overlapping aspects of nociceptive, neuropathic, and nociplastic pain, should lead to more precise and individualized management of this growing population.

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IS-16

Keynote Lecture: Neuro-immune mechanisms of pain in fibromyalgia

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Fibromyalgia is a debilitating widespread chronic pain syndrome that occurs in 2-4% of the population. The prevailing view that fibromyalgia results from central nervous system dysfunction has recently been challenged with data showing changes in peripheral nervous system activity. We used a hyperalgesic priming paradigm and a back-translational model in mice to demonstrate the pro-nociceptive role of neutrophils in causing chronic widespread pain in fibromyalgia. Adoptive transfer of neutrophils from mice with chronic widespread pain or from patients with fibromyalgia can confer mechanical pain to recipient naïve mice, sensitise evoked action potential firing of spinal cord neurons and produce phenotypic changes in cell surface expression of neutrophil proteins that cause infiltration of neutrophils into dorsal root ganglia. These data provide the framework for an immunological basis of chronic widespread pain in fibromyalgia mediated by polymorphonuclear granulocytes.

IS-17

From painful joints to widespread pain: why is fibromyalgia so common in rheumatoid arthritis?

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Fibromyalgia was a controversial diagnosis when the American College for Rheumatology (ACR) published the first classification criteria in 1990 (1). Over the last decade, the importance of recognising fibromyalgia has been acknowledged in international recommendations as many studies including systematic reviews have shown that fibromyalgia is common in patients with inflammatory arthritis. In rheumatoid arthritis (RA), 1 in 5 patients has concomitant fibromyalgia (2). Not only the condition is prevalent, but patients with concomitant fibromyalgia have higher disease activity scores such as DAS28 (2) resulting in clinicians switching treatment on the basis of treat-to-target. This is recognition in the European Alliance of Associations for Rheumatology points to consider in the management of difficult to treat RA (3). It highlighted that the concomitant fibromyalgia could lead to moderate or high disease activity without evidence of inflammation. Indeed, in the 2016 revised ACR diagnostic criteria, fibromyalgia is no longer a diagnosis of exclusion and acknowledge that fibromyalgia can occur in the presence or absence of many rheumatic diseases. This opens the possibility that fibromyalgia may be secondary to RA.

Even though the secondary fibromyalgia is unproven, prospective study of early RA from the time of diagnosis suggested that the incidence of fibromyalgia may be higher than expected than the general population. There are several potential mechanisms through which fibromyalgia may develop in patients with RA (5). First, cytokine receptors of tumor necrosis factor alpha, interleukin (IL) 1 and IL-6 are expressed by sensory nociceptive neurons, dorsal root ganglia and central nerve system. These inflammatory cytokines have been shown to induce allodynia in models of neuropathic pain and inflammatory arthritis. In RA, anti-IL-6R monoclonal antibodies (6) and Janus kinase inhibitors (7) have been shown to reduce pain more than expected than through reducing inflammation. Second, repeated stimulation of sensory neurones can reduce threshold and amplitude of signals, a phenomenon known as temporal summation or windup, so can cause hyperalgesia and allodynia. Lastly, poor quality sleep and mental well-being associated with RA can impair descending pain inhibitory mechanism.

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IS-18

SLE and chronic pain

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Systemic Lupus Erythematosus (SLE) is a multisystemic autoimmune disease characterised by tolerance breakdown and consequent expansion of autoreactive clones of B and T cells that are responsible for autoantibodies production. SLE clinical features are based on a variety of symptoms such as the presence of fever, arthralgia, skin rashes, and pain or joint swelling. Other symptoms may include sun sensitivity, oral ulcers, arthritis, multiorgan involvement, especially kidneys, blood cells and immunological abnormalities. Chronic pain is a frequent symptom reported in SLE patients. Pain is located mainly in the musculoskeletal system and is related to joint arthritis, while headache, generalised pain, and abdominal pain may be more closely associated with fibromyalgia. Furthermore, reduction in physical activity and the concomitant use of glucocorticoids and immunosuppressants may worsen the sense of fatigue perpetuating the cycle of chronic pain. Given the complexity of the disease, it is important to identify effective therapeutic approaches for the treatment of chronic pain, especially to improve the quality of life of affected patients.

IS-19

Sjögren's syndrome and fibromyalgia

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Sjögren's syndrome (SS) is an autoimmune systemic disease caused by immune inflammation of the exocrine glands. Glandular cell destruction and impaired secreting function together produce symptoms such as xerophthalmia and mucosal surface dryness, however other symptoms like pain and fatigue are very common (1). Pain in SS is attributed to nociceptive and neuropathic factors, and pain-related diseases such as fibromyalgia (FM) are prevalent in SS (2). SS showed the highest prevalence (62%) of chronic overlapping pain conditions (2). In the Mayo Clinic database of 13,849 SS, 5.6% had FM at SS diagnosis. Notably, during the follow-up, the top comorbidities in patients with SS were FM (25%), depression (21.2%) and pain (16.4%), women being at higher risk (3). Similarly, in the French cohort, prevalence of FM is around 20% (4). Patients with FM showed higher ESSPRI score, as expected, but not higher ESSDAI score (4), supporting previous evidence that widespread pain associates with a lower prevalence of autoantibodies and extraglandular manifestations in SS (5). A 14.6% of FM prevalence was found in the Spain registry, where these patients significantly showed more constitutional, fatigue and arthralgia symptoms (6). Moreover, FM is an independent contributor to fatigue in SS (7).

Considering the common symptoms shared by FM and SS, the association between the two has long been debated. Patients with FM have significantly increased prevalence of xerostomia, glossodynia, dysphagia, and dysgeusia (8). Previous research has suggested that SS may play a role in the pathophysiology of FM (12). The role of inflammation is controversial in FM, and the involvement of autoimmunity in the pathophysiology of FM has not been completely understood, due to the presence of autoantibodies in FM, such as anti-SS-A/Ro, anti-SS-B/La, ANA, or RF, typically demonstrated in the blood in the pre-clinical stage of SS (9). Indeed, disturbances of the neuroendocrine axis have been claimed for both the diseases (10, 11). Finally, a greater prevalence of FM was documented in HTLV-I infected individuals, suggesting that FM may be linked with this virus, which shows tropism for the salivary glands sometimes mimicking Sjögren's syndrome-related parotid swelling (12).

Interestingly, taking comorbidities into account, FM is one of the most important conditions that can predict SS (OR 2.50 [1.93-3.25]) in a model including also osteoporosis, hormone replacement therapy, diabetes, and body mass index (13). This risk was confirmed by a recent population-based study on 149,706 subjects whose 74,853 with FM. The aHR was 2.00 (95% Confidence Interval [CI], 1.52-2.61) for developing SS, with patients aged 20-49 years showing the highest risk [3.07 (95% CI, 1.92-4.89)] (14).

Small fibre neuropathy, a condition characterized by chronic pain, hyperalgesia and dysesthesia is a rare neurological manifestation in SS that can be the first presentation of the disease (15).

Thus, in SS it is very important to differentiate chronic pain due to FM or due to small fibre neuropathy. In small fibre neuropathy pain is related to loss or dysfunction of intraepidermal small nerve fibres, and neurological symptoms include paraesthesia, allodynia, sicca symptoms, warm or cold hypoesthesia whereas headache points toward FM (16).

Treatment for both SS related symptoms and FM still remain an open issue in the research agenda. Even if some biologic agents are demonstrating such an improvement in the systemic disease activity in SS, symptoms including fatigue and pain, are still unaffected (17).

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IS-20

Taking a closer look at the use of hyperbaric oxygen therapy for fibromyalgia

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Fibromyalgia Syndrome (FMS) is currently considered to be a prototype of nociplastic pain – conditions, in which pain is attributed to aberrant processing within the central nervous system, rather than to peripheral damage to tissue or nerves. The insights that FMS is caused by real biological dysfunction in certain brain regions, calls for new biological interventions that can induce neuroplasticity- repairment of the nonfunctioning brain regions.

Clinical studies done in recent years present convincing evidence that the new protocols of hyperbaric oxygen therapy (HBOT) can be the coveted neurotherapeutic treatment for neurological incidents like stroke, traumatic brain injury, PTSD and fibromyalgia. This new understanding leads to a paradigm change in the way that we refer to chronic brain injuries; from now these should be thought of like other non-healing wounds in other parts of the body (*e.g.* non-healing leg ulcers). Even though many of the beneficial effects of HBOT can be explained by the improvement of tissue oxygenation, it is now realized that intermittent increase of oxygen concentration can induce many of the mediators and cellular mechanism that are usually induced during hypoxia but without the hazardous hypoxia, termed “The Hyperoxic-Hypoxic Paradox” - HHP. HHP is a newly suggested paradigm aiming to enhance the endogenous repair mechanisms, while providing an optimal microenvironment. By utilizing repeated intermittent hyperoxic exposures, hypoxia-triggered mediators and cellular mechanisms are paradoxically induced without hypoxia. These effects include stem cells stimulation, migration and differentiation, mitochondrial proliferation/biogenesis, mitochondrial transfer and angiogenesis.

Those far, seven clinical studies evaluating the effect of HBOT on FMS patients reported positive results. In this lecture we will discuss the mechanisms and long-term biologic effect of HBOT relevant for FMS patients. In addition, the already published studies will be reviewed and new additional data from studies that are currently under review will be presented and discussed.

IS-21

Manipulating the microbiome as a potential new therapeutic strategy for chronic pain

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The growing appreciation of the importance of the gut microbiome in health and disease is revolutionizing many fields of clinical medicine. In recent years we focused on the role gut bacteria play in the pathogenesis of fibromyalgia. In fibromyalgia, the composition of the gut microbiome of affected women shows significant alterations as compared to healthy controls, as certain bacterial taxa are found at either increased- or decreased abundance. Furthermore, differences in the metabolic activity of gut bacteria are associated with altered circulating metabolic end-products in the blood of women with fibromyalgia. Finally, transplantation of gut bacteria from women with fibromyalgia, but not from healthy controls, to germ-free mice led to pain hypersensitivity. Taken together, gut microbiome composition is compositionally associated with fibromyalgia, its function is altered in women with fibromyalgia and finally, it seems to play a causal role in the pathogenesis of the syndrome. These recent observations pave the way for the development of much-needed new diagnostic and therapeutic modalities for fibromyalgia and possibly other forms of chronic pain, which will be discussed.

IS-22

The ongoing role of anti-depressants and anticonvulsants in fibromyalgia

Winfried Häuser
Winfried Häuser is specialist of general internal medicine, psychosomatic medicine and pain medicine. He is author of systematic reviews of pharmacological and non-pharmacological treatments of FMS. His H-index is 90

Fibromyalgia syndrome (FMS) is regarded to be the prototype of a nociplastic pain condition. Central sensitization on the levels of thalamocortex, descending brain stem and spinal cord is assumed to be the main pathophysiology mechanism of FMS. Some anticonvulsants and antidepressants may act on these three levels of the central nervous system. It has been demonstrated that short term treatment with pregabalin altered brain structure and evoked-pain connectivity and these decreases were associated with less clinical pain in patients with FMS.

Because of their effects on mood, these classes of medication can also modify potential affective and cognitive amplifiers of pain experience. In the communication with patients these medications should be labelled "central pain modulators".

The serotonin noradrenaline reuptake inhibitors (SNRIs) Duloxetine and Milnacipran and the anticonvulsant pregabalin have been approved by the Food and Drug Administration (FDA) but not the European Medicines Agency (EMA) for the management of FMS. One European study each of these three medications missed to reach the primary endpoint (superiority in mean pain change from baseline). There are no statistically relevant differences between these three medications in pain relief. Yet, only pregabalin has a clinically relevant effect on fatigue and none of these medications has a clinically relevant effect on fatigue. The "historical" studies with tricyclic agents (mainly amitriptyline) and some serotonin reuptake inhibitors (SSRIs) (citalopram, fluoxetine, paroxetine) suggest a comparable efficacy on pain and a better tolerability (lower rate of drop outs due to side effects) compared to the FDA-approved medications. However, the studies with TCAs and SSRIs have a very low methodological quality.

Not every antidepressant or anticonvulsant is effective against FMS-pain. There was one negative study each for the SNRI desvenlafaxine (n=125 patients), Levetiracetam (n=66 patients), lacosamide (n=162 patients) and eslicarbazepine (n=529 patients) and three negative studies with n=591 patients with mirtazapine, a noradrenergic and specific serotonergic antidepressant (NaSSA) which is also labelled to be tetracyclic antidepressant. Duloxetine, milnacipran and pregabalin are not the holy grail of pharmacological treatment of FMS. Medication with other mechanisms of action than modifying central processing of stimuli might be effective. Three studies with 1309 patients have been conducted with sodiumoxybate, the sodium salt of gamma-hydroxybutyrate which is licensed for narcolepsy. The relief

of pain and sleep problems was better than with duloxetine, milnacipran and pregabalin but the drop out rate due to side effects was higher. Due to safety concerns, sodiumoxybate was not approved by EMA and FDA. We hope that the ongoing studies with naltrexone (an opioid antagonist) and cannabis-based medicines will show efficacy and safety and will enlarge the options of the pharmacological treatment of FMS.

IS-23

Rational implementation of Jak inhibitors and other biologics in treating chronic pain and fatigue

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Chronic pain and fatigue are prevalent health conditions that significantly impact the daily lives of millions of individuals worldwide. Conventional treatments, such as pain medications and physical therapy, have not provided lasting relief for many patients. Inflammation is a critical mechanism underlying the development of these conditions, particularly in the case of chronic fatigue associated with rheumatoid arthritis (RA). Jak inhibitors, a class of biologic drugs, have emerged as a promising alternative for managing chronic pain and fatigue by targeting these underlying inflammatory mechanisms, having shown great potential for modulating immune system function and reducing inflammation, which are key drivers of chronic pain and fatigue (1).

Jak inhibitors act by blocking the activity of Janus kinases (JAKs), enzymes involved in the signaling pathways that regulate immune system function and inflammation (2). Therefore, by inhibiting JAK activity, Jak inhibitors can reduce inflammation and modulate the immune system, leading to a reduction in chronic pain and fatigue symptoms. However, it is still unclear whether they could be of help in patients with RA or other inflammatory systemic diseases (3-5).

The use of Jak inhibitors and other biologics in treating chronic pain and fatigue requires a well-considered and individualized approach. A thorough evaluation of the patient's medical history and physical examination is essential to determine the underlying causes of pain and fatigue and to rule out any potential contraindications. Once a diagnosis has been made, treatment should be tailored to the patient's specific needs and the severity of their symptoms.

In addition to close monitoring for potential side effects, it is important to consider biologics in conjunction with other treatments, such as physical therapy, and in coordination with the patient's primary care physician. With proper evaluation, individualized treatment planning, and close monitoring, biologics can provide effective relief for many patients suffering from chronic pain and fatigue (6).

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IS-24

Acetyl L-carnitine (LAC) and Palmitoylethanolamide (PEA): Nutritional supplements in the struggle against chronic pain

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According to the International Guidelines, Fibromyalgia Syndrome (FMS) treatment should be based on multimodal rehabilitation programs, psychological and pharmacological treatments (1). However, to date, no medication has been shown to significantly improve pain, associated symptoms and Quality of Life (QoL) of FMS patients. For this reason, there is a strong need for new effective and safer compounds, especially when used as a long-term treatment. Recent evidence has emphasized the role of microglia and mast cells in generating and maintaining pain in FMS. Moreover, oxidative stress was also considered as a part of the pathophysiological picture in FMS patients, with an imbalance between systemic oxidants levels and antioxidant ability. Lastly, FMS patients showed high prevalence psychological disturbance like depressive mood, anxiety, bipolar disorder, drug abuse, and others (2). PEA is well known to down-modulate mast cells activation and to control the microglial cell behaviours, thus reducing inflammation and pain. LAC has demonstrated antioxidant properties, modulates brain neuro-transmitters serotonin and dopamine, acts as neurotrophic factor and increase metabotropic glutamate receptors type 2 (mGlu2) through an epigenetic mechanism. LAC reduce the oxidative-stress markers concentration (*i.e.* glutathione), and inhibit the release of pro-inflammatory cytokines (IL1- β , TNF- α) in the activated microglia thus reducing the development of neuroinflammation. The increase of mGlu2 receptors leads to analgesia, counteract spinal sensitisation and improve depression and antidepressant drug efficacy.

At our Pain Centre, we investigated the role of ultramicrozoned-PEA (um-PEA) and LAC as add-on treatment in FMS patients. In a retrospective observational study, we administered um-PEA to 407 patients. Data of these patients were collected until 15 months after the first drug prescription. In this population, a moderate long-lasting and statistically significant pain relief was observed, with a reduction of VAS score from 75.8 \pm 0.8 at baseline to 52.5 \pm 1.7 at 15 months with a significant improvement in QoL measured by Fibromyalgia Impact Questionnaire (FIQ). Only a minority of patients reported adverse events predominantly of gastrointestinal type (diarrhoea, dyspepsia, bloating, constipation, vomiting) (3). In a recent prospective observational study, we administered LAC to 253 FMS patients then followed for 15 months. Also in this observation, preliminary data analysis showed a moderate but significant reduction in VAS and FIQ scores in the majority of patients, until the end of follow up, with a low incidence of adverse events, predominantly nausea and restlessness (4). In conclusion, PEA and LAC showed in our experience a moderate but significant improvement in pain and QoL in our FMS population. Future research may corroborate these findings.

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IS-25

Classifying (and misclassifying) fibromyalgia: why definitions make a difference

Winfried Häuser

Winfried Häuser is specialist of general internal medicine, psychosomatic medicine and pain medicine. He was the head of the steering committee of the German guidelines on fibromyalgia and member of the steering group of the EULAR recommendations on the management of fibromyalgia. His H-index is 90.

The World Health Organization (Who) 11th revision of the International Classification of Diseases (ICD-11) has come into effect in February 2022. ICD-11 pretends to improve the clarity of terms for the general public and to facilitate the coding of important details such as the spread of a cancer or the exact site and type of a fracture. There is a flexible transition period of 5 years. No later than 2027, national reports on mortality to the WHO have to use the ICD-11. There are no fixed dates when ICD-11 will be used on a national level for coding of mortality.

A small interdisciplinary working group of the International Association of the Study of Pain (IASP) has developed a classification system for chronic pain for ICD-11. A new chapter "Symptoms, signs or clinical findings, not elsewhere classified" was created. This chapter makes a distinction between chronic primary pain ("disease of its own right") and chronic secondary pain (pain as a symptom of a defined disease). FMS has been classified as chronic primary pain as a subgroup of chronic widespread pain. FMS has been removed out of the chapter "Diseases of the musculoskeletal system or connective tissue" and can be only coded in the chapter "Symptoms, signs or clinical findings, not elsewhere classified". All other so-called primary pain syndromes such as migraine or irritable bowel syndrome have remained in their previous chapters. The original proposal of the IASP group to define FMS as chronic widespread musculoskeletal pain was abandoned – as a compromise with some psychiatrists in the WHO which intended to eliminate the diagnostic label "FMS" in the ICD. The new classification system with regards to FMS was not broadly discussed in the pain community and not at all with other medical associations and FMS self-help organisations. A small group within IASP has taken the ownership on the definition and classification of FMS in the ICD-11.

The main concern with the classification of FMS in ICD-11 is that FMS has no more a diagnostic code of its own in ICD-11 - in contrast to ICD-9 and ICD-10. However, (early) diagnosis and specific therapies need diagnostic codes. In countries, where ICD code use is obligatory, treatment reimbursement can become difficult. Health care services with data of statutory health insurance companies in countries which require ICD-codes will no longer be possible.

In addition, there are some conceptual problems with the new definitions of CWP and FMS (*e.g.* why isn't FMS defined as chronic primary musculoskeletal pain?) which will be outlined in the lecture.

FMS-experts have published their concerns on the definition and classification of FMS in ICD-11:

HÄUSER W, CLAUW DJ, WOLFE F, SARZI-PUTTINI P, ABLIN JN, USUI C, LITTLEJOHN GO, MORLION B, KOSEK E, FORS EA, ØIEN FORSETH KM, FITZCHARLES MA: Concerns about the taxonomy, definition and coding of fibromyalgia syndrome in ICD-11: the potential for negative consequences for patient care and research. *Clin Exp Rheumatol* 2022; 40: 1073-75.

They have submitted these proposals for changing the definition of FMS to the ICD-11 platform of the WHO:

- FMS should have a code of its own in the category chronic primary pain in ICD-11.
- FMS should be arranged into the subcategory "Primary musculoskeletal pain" and defined as "primary widespread musculoskeletal pain".
- FMS should also have a code in the chapter "Diseases of the musculoskeletal system or connective tissue"

IS-26

The role of patient associations

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Patient Associations are non-profit social utility organizations. They are engaged both in activities of collective interest and in the protection of individual patients, working to ensure them a better quality of life in terms of medical, pharmacological and social assistance.

Fibromyalgia Patients' Associations create and develop dedicated programs for the improvement of fibromyalgia patients' lives. One of these Patient Associations is Aisf-Odv (Italian Association of Fibromyalgia Syndrome), which was born in 2005 in Milan, but operates throughout the national territory. Our Patient Association created a nation-wide Network able to directly support patients, listening to them and educating them to actively self-manage their condition: these interventions were shown to be particularly effective in many chronic conditions, especially in fibromyalgia, and self-management programmes have been at the core of many interventions (1, 2).

This is done through educational interventions about the disease (which are organized not only for patients, but also for healthcare professionals and Institutions), various workshops and activities. Examples of such activities are the Art therapy workshop, which helps patients transform their suffering with a greater and more correct awareness, movement activity projects and psychoeducational support groups. A recent nation-wide, ambitious project is to build up Reference Centres for the multidisciplinary management of fibromyalgia syndrome.

In Italy, fibromyalgia syndrome is not recognized as a chronic and disabling disease at an institutional level.

Patient Associations' main objective is to ensure this recognition, in order to give dignity to those who suffer from this condition, who very often are not even believed to be ill.

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IS-27

The role of registries in fibromyalgia

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While data from randomized controlled clinical trials represent the best of scientific evidence, in the context of chronic conditions such as fibromyalgia there is an increasing need to obtain real-life data. With the information technology available today, it is possible to simplify the data collection process, apply it on a large scale in a uniform manner by organizing it into a registry. A registry is defined as "an organized system that uses observational study methods to collect uniform data (clinical and other) to assess specific outcomes in a population defined by a particular disease, condition or exposure, and that serves a predetermined scientific, clinical or policy purpose."

Several registries exist for fibromyalgia worldwide. However, until the creation of the Italian Fibromyalgia Registry (IFR), there were no European registries for this condition. The creation of the IFR was supported by both the Italian Society of Rheumatology ("SIR") and the Italian Ministry of Health. The IFR, to date includes over 54 Italian centers and over 6500 patients. IFR has essentially enabled the achievement of multiple objectives, the main ones of which can be summarized as: 1) to assess and monitor patients' conditions over time through demographic data, clinical descriptors, and uniform outcome measures estimated with standardized and validated tools at each participating site; 2) to establish disease severity cut-off points to support health care decision-making and optimize clinimetry; 3) provide

researchers with reliable, real-world data to answer important research questions, test hypotheses related to various aspects of chronic widespread pain and its management, assess study feasibility, and facilitate patient recruitment into clinical research; 4) support research projects by promoting cooperation among centers and assisting in the implementation of research projects.

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IS-28

Patient-Centred care for Fibromyalgia – New pathway Design (PACFiND)

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The 2017 European Alliance of Rheumatology Associations (EULAR) recommendations for fibromyalgia provided evidence-based approaches to effective care. While these considered individual management approaches, it was not that there was very little research focussed on how these combined into effective pathways of care. Indeed, a subsequent review on this topic noted that there was no evidence-based approaches to organising healthcare which covered the entire care pathway, however there was some evidence that long-term management in secondary care did not result in better outcomes (Doebel *et al.* 2020). We set out in the PACFiND project to design a patient-centred and evidence approach to healthcare. This presentation will include a survey of health care professionals in relation to what care they provide (and how they provide it); a survey of patients in relation to what care they access outside the National Health Service (Wilson *et al.* 2022). We will compare the impact of symptoms (and experience of health) amongst those who have received a diagnosis of fibromyalgia; those who meet criteria for fibromyalgia but who have not received a diagnosis; patients who have chronic pain but not fibromyalgia (Doebel *et al.* 2022). Data linkage has allowed us to characterise patients with a code for fibromyalgia within part of the UK health system in relation to, for example, comorbidities, prescribed medication and use of health services and these allow us to describe how patients interact with healthcare. Together with a series of videos produced for and by patients (healthtalk.org) case studies from care teams throughout the United Kingdom and health economic studies, we will describe how these will come together to propose a new model of care for people with (or under investigation for) fibromyalgia.

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Classification, diagnosis, epidemiology and the evolving concept of fibromyalgia**P-01****Gastrointestinal disorders in fibromyalgia subjects**

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Background. Fibromyalgia (FM) is characterized by chronic generalized pain. Its etiology is not completely understood at present and there are few effective treatments.

Objective. The aim of this study was to investigate a possible relationship between chronic pain and gastrointestinal disorders (GID) with particular attention to the presence of GID in FM patients.

Methods. Chronic pain patients (n=122) were enrolled; n=103 suffered FM, n=19 suffered other chronic pain (CP) syndromes. 92% were females, 8% males. Self-administered questionnaires were used: Global Assessment of Improvement Scale (GAI) and Symptom Severity Scale (SSS) to assess GID; Visual Analogue Scale (VAS) to measure pain intensity; Widespread Pain Index (WPI) to quantify the extent of widespread pain throughout the body; Symptom Severity (SS) scale to assess features of centralized pain in subjects with painful conditions.

Results. VAS was higher in FM than CP (6.8 vs. 4.6, p0.001). WPI was 13.9 and SS 7.2 in FM subjects. GID was reported by 75 of the FM patients and by 4 of the CP ones. GAI was lower (worse) in FM than in CP subjects (30.35 vs. 41.00).

Conclusion. Subjects with FM have a high prevalence of gastrointestinal complaints that should be carefully assessed due to the possible effect of GI conditions on health. Appropriate treatment of GID would improve the patients' symptoms, although this approach requires further study.

P-02**Diffusion tensor imaging of white matter microstructure in fibromyalgia: a pilot study**

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Background. Magnetic resonance (MR) studies provided initial data indicating chronic pain might lead to changes in brain structure and function.

Objective. To analyze MR Diffusion Tensor Imaging quantitative parameters in patients with fibromyalgia, in order to identify significant microstructural alterations in brain areas and circuits implicated in pain chronicity.

Methods. Fourteen consecutive patients with clinical diagnosis of fibromyalgia (females, mean age 54.21±8.71 years) and 9 age-matched healthy controls (females, mean age 51.67±6.85 years) underwent diffusion tensor imaging using a 1.5 Tesla system. Fractional anisotropy (FA), mean diffusivity (MD), axial diffusivity (AD) and radial diffusivity (RD) values were calculated using region of interest atlas-based tract-mapping in 13 cerebral areas, and compared among the two groups.

Results. Mean FA values were significantly lower for the fibromyalgia group than for the control group in the Nucleus Accumbens, in the fiber tract between Nucleus Accumbens and orbito-frontal cortex, in the pallidum, in the posterior internal capsule, in the insula, and in the cingulum (p0.05). We also observed significant differences in mean RD values in the hippocampal tail and in mean MD and AD in the cingulum.

Conclusion. Our findings suggest that diffusion tensor imaging may provide a non-invasive biomarker of white matter changes in fibromyalgia patients. Nucleus Accumbens and its connection fibers, as well as insula and cingulum, seems to be the best sites to analyze. Further studies are needed to confirm their role in chronic pain and as potential therapeutic target in these patients.

P-03**Characterizing individuals with fibromyalgia in symptom severity, pain severity, sensory responsiveness, cognitive self-efficacy, and perceived general health**

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Background. Fibromyalgia (FM) is characterized by chronic widespread pain, accompanied by physical, emotional, and cognitive dysfunction, severely affecting daily function and quality of life (QOL). Yet FM is under-diagnosed and while constituted as a primary pain disorder, its similarities with rheumatoid arthritis (RA) may compromise treatment.

Objective. To better understand the FM phenomenon by comparing symptom severity, pain severity, sensory responsiveness, cognitive self-efficacy (CSE), and perceived general health in people with FM vs. RA, and analyzing qualitative data regarding daily experiences of those with FM.

Methods. Cross-sectional mixed-method study including 213 women [n=179, aged mean (SD) 43.80 (13.48)] and men [aged mean 40.77 (12.53)] with FM (n=194) or RA. Participants filled out an online survey consisting of (1) Socio-Demographic data, (2) Fibromyalgia Impact Questionnaire, (3) Brief Pain Inventory, (4) Sensory Responsiveness Questionnaire, (5) Cognitive Self-Efficacy Questionnaire II, (6) Self-Rated Health, and (7) Open-ended questions developed for this study.

Results. Compared to RA, people with FM report worse symptom severity (p=0.002), greater pain severity (p=0.000) and impact (p=0.000), greater sensory over-responsiveness (p=0.000), worse CSE (p=0.002), and worse self-rated health (p=0.002). CSE was found to predict FM group placement (OR=0.36; p=0.03). Qualitative analysis from 104 respondents in the FM group identified "living with FM" as the main theme, yielding four main categories encompassing daily function and difficulties.

Conclusion. Findings contribute to better characterizing FM. This is the first study to quantify SMD and investigate cognitive self-efficacy in people with FM. It may be suggested to address these when treating people with FM.

P-04**Could *Dysosmobacter Welbionis* be a modulable biomarker in specific fibromyalgia patients?**

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Background. Fibromyalgia (FM) is a widespread chronic disease characterized by chronic pain. Since FM patients present several gastrointestinal disturbances, the relationship between microbiota and FM could be a promising field to explore. When the microbiota distribution is altered, intestinal dysbiosis appears and the majority of the related conditions are strongly connected to FM. As a result, it would be interesting to look for intestinal markers in FM patients in order to improve its diagnostic and therapeutic approach.

Objective. To identify modulable biomarkers in the intestinal microbiota of FM patients to improve their quality of life.

Methods. A group of 210 women diagnosed with primary FM according to ACR and 40 healthy women as controls were selected. Intestinal microbiota composition was identified by sequencing the 16S rRNA gene using Illumina technology. Additional data such as SF-36 health questionnaires, BMI and other comorbidities was also collected.

Results. Several bacterial species have been identified. Among them, *Dysosmobacter welbionis* showed a marked decrease in FM, even low in those patients with metabolic syndrome. Strikingly, *D. welbionis* has been proposed as a protective bacteria in type 2 diabetes, since it seems to increase the number of mitochondria and reduces inflammation, useful features in FM. Furthermore, this specie correlates positively with the score in health questionnaires.

Conclusion. The lower abundance of *D. welbionis* found in FM patients, especially in those with metabolic syndrome, could be a therapeutic target to improve the chronic pro-inflammatory state and the mitochondrial energy imbalances in these FM patients.

P-05

Middle East pain syndrome is a pollution-induced new disease mimicking rheumatoid arthritis

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Musculoskeletal pains are sometimes misdiagnosed in some diseases, like rheumatoid and psoriatic arthritis, erosive OA, etc. Secondary hyperparathyroidism was not considered a differential diagnosis for RA, despite the fact that it can cause arthralgia or arthritis. Also, fibromyalgia is a psychosomatic condition marked by widespread pain and tenderness. This study included 400 patients attended certain outpatient clinics of Rheumatology in Egypt and Saudi Arabia, who were not fulfilling criteria for RA diagnosis. Criteria for classification of fibromyalgia syndrome were applied to all patients. We did lab tests and radiological imaging modalities for diagnosis or exclusion of suspected diseases were applied. All patients were fulfilling both old and new criteria of fibromyalgia syndrome, and not fulfilling any RA criteria, and had vitamin D3 deficiency or insufficiency. 75% of patients had abnormally high levels of PTH, without parathyroid gland pathology. Radiology showed subperiosteal and subchondral resorption of mainly thumbs, subchondral osteopenia of proximal and middle phalanges, mild subperiosteal resorption along the radial aspect of the middle phalanx and mild tuft erosions, besides changes in the carpus closely resembling those of rheumatoid arthritis, of ulnar styloid resorption, radiocarpal and scapho-trapezoid joint arthritis. Of special interest, the presence of tuft spur-like excrescences.

P-06

Comorbid associations in fibromyalgia. Looking beyond irritable bowel syndrome: findings from an investigation into Fibromyalgia, Digestive Function and the Microbiome of the Gastrointestinal Tract (the FIDGIT study)

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Fibromyalgia is a poorly understood condition with common comorbidities. These include but are not limited to migraine, depression, functional gastrointestinal disorders (FGID), and chronic fatigue.

The relationship between fibromyalgia and irritable bowel syndrome (IBS) is well known, however, the prevalence of the broader group of FGIDs has received little attention.

The purpose of this study included characterising the health status of people living with fibromyalgia, including gastrointestinal function and co-morbidities, and compare them to healthy controls.

We recruited women with fibromyalgia and healthy controls. Data was collected via validated instruments (including Rome IV, ACR 2016), online surveys, in-clinic assessments, physical assessment, and biological samples. In addition to fibromyalgia, 106/113 women (93%) reported a total of 360 comorbid conditions at recruitment, compared to 37 conditions in 24/55 (43%) of controls. Fifty-one women with fibromyalgia (45%) shared 60 known gastrointestinal pathologies, 65% of these (39) were diagnosed IBS. Our evaluation identified 354 FGIDs in 106/111 (95.5%) participants, whereas the total FGID burden in the control group was 31 disorders in 20/55 women (36%).

Less than 15% of the detected FGIDs had been formally diagnosed.

The broader group of FGIDs may be much more prevalent in fibromyalgia than previously appreciated, indicating a significant degree of gastrointestinal dysfunction. Whether the FGIDs relate to alterations of the gut microbiome, and how that may affect symptom presentation is yet to be evaluated this cohort. Our data support the hypothesis that fibromyalgia is a multi-system illness and future research should expand on this theory.

P-07

Why does it hurt so much? Emotion regulation mediates the association between fibromyalgia symptoms and psychological distress

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Background. While it is known that fibromyalgia patients often suffer from depression and stress, there is inconclusive evidence as to why these symptoms occur.

Objective. The aim of this study is to examine the role of emotion regulation in mental health symptoms among treatment-seeking Fibromyalgia patients. **Methods.** Ninety-three (93) treatment-seeking Fibromyalgia patients (mean age=47.25, SD=12.4) were recruited from one of Israel's largest community healthcare providers.

Fibromyalgia patients were administered self-report questionnaires assessing Fibromyalgia symptoms (FIQR), perceived stress (PSS), major depression (PHQ-9) and difficulties in emotion regulation (DERS).

Results. Associations were found between measures of Fibromyalgia, psychological distress, and emotion regulation. Sub-indices of emotion regulation showed significant correlations to mental health, except for Lack of emotional awareness and Lack of emotion clarity. Non-acceptance of emotional responses showed the strongest correlations. Moreover, Non-acceptance of emotion responses mediated the association between Fibromyalgia symptoms and psychological distress.

Conclusion. Our findings show that the connection between Fibromyalgia symptoms and psychological distress partially explained by emotion regulation. Moreover, we show that specific emotion regulation strategies play a differential role in Fibromyalgia patients' distress, thereby highlighting the importance of emotion regulation as a therapeutic target. Specifically, regulating through acceptance of emotional responses seems to be particularly important for Fibromyalgia patients.

P-08

Alexithymia and psychological distress in fibromyalgia and chronic migraine: Clues for nociplastic pain conditions?

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Background. The concept of nociplastic pain (NP) may represent a new framework to understand similarities among different pain conditions. Several studies have shown a strong association between alexithymia and psychological distress in different chronic pain conditions.

Objective. To investigate the prevalence and association between alexithymia and psychological distress in individuals with fibromyalgia (FM) and chronic migraine (CM) compared with healthy controls (HC).

Methods. A cross-sectional study was conducted. Two hundred and fifty women with FM (age: 51.2±10.5) and 250 women with CM (age: 46.1±11.5) were assessed with the Toronto Alexithymia Scale (TAS-20) and the Hospital Anxiety and Depression Scale (HADS) vs. HCs (n=280; age: 51.8±9.0) by one-way analyses of variance. A moderation analysis was performed as well.

Results. Differences between groups showed significantly higher scores for TAS-20 [F(2,755)=11.7, p=0.001] and HADS [F(2,763)=31.7, p=0.001] in FM, compared with CM and HCs. The moderation analysis showed that both clinical groups and TAS-20 (β=0.20, p.001) were significant predictors, as well as the interaction terms. The slope of the correlation curve was more pronounced in the patient groups, indicating that the degree of alexithymia had a significantly higher influence on the HADS total score in the patient groups.

Conclusion. The results suggest a common psychological dysregulation in FM and CM, with a slight but greater prevalence of alexithymia and psychological distress in FM. The concept of NP opens to a new framework for understanding the co-occurrence of different chronic disorders and the role of related psychological factors.

P-09

Detailisation of pain in patients with ankylosing spondylitis

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Objective. To evaluate the incidence and manifestations of FM in patients with AS.

Methods. 40 patients with AS were studied. The average age is 43±14.05 [34.5;50.5]. Disease activity (ASDAS): high - 85%, moderate - 5%, low - 10%. Functional insufficiency (FI): 45% - 3 degrees, 25% - 2 degrees, 30% - 1 degree. The median duration of illness was 114 [66;144] months. Clinical examination included: assessment of neuropathic pain (NP) according to the Pain detect (PD), the fibromyalgia (FM) - FIRST, quality of life - EQ-5D questionnaires.

Results. All patients had inflammatory pain in the back, 80% - had non-inflammatory pain: NB (PD) - 65%, FM (FIRST) - in 50% (with a predominance of the cognitive component). Direct relationship was FM, NP with age. There was a direct correlation of FM (FIRST) with disease activity (ASDAS) (rSp=0.587; p=0.008), FI (rSp=0.615; p=0.004) and pain intensity (VAS) (rSp=0.751; p=0.001), revealed strong feedback with the EQ-5D index (rSp=-0.672; p=0.001). 65% of patients had comorbid pathology (anemia, arterial hypertension (AH), osteoporosis). Direct correlation was found between the indices PD (rSp=0.569; p=0.009), FIRST (rSp=0.615; p=0.004), the presence of hypertension - PD (rSp=0.507; p=0.023), FIRST (rSp=0.524; p=0.018), and anemia (rSp=0.715; p=0.001) for FM.

Conclusion. 50% patients with AS had FM, with a predominance of the cognitive component. In the presence of FM, activity is higher, hypertension and anemia are more common, and the quality of life is worse.

P-10

The multicomponent nature of pain in patients with rheumatic diseases

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Rheumatological patients have mixed genesis of chronic pain.

Objective. Rheumatological patients have mixed genesis of chronic pain. We aimed to study the specifics of pain in patients with rheumatoid arthritis and ankylosing spondylitis.

Methods. 78 patients were studied: 30.8% of patients with rheumatoid arthritis (RA) and 68.2% with ankylosing spondylitis (AS). Disease activity was assessed using the DAS28 and BASDAI/ASDAS scales. Clinical examination included: assessment of neuropathic pain (NP) according to the Pain detect (PD), the fibromyalgia (FM) - FIRST, quality of life - EQ-5D questionnaires.

Results. All patients had chronic inflammatory pain in the back, 69.3% - had non-inflammatory pain: NP(PD) - 38.4%, FM(FIRST) - 50% (with a predominance of the cognitive component). NP prevailed in patients with RA, FM - in patients with AS. 53.9% of patients had a positive result on the NP(PD): 41.2% - AS, 87.5% - RA. There was a direct correlation of the NP(PD) with laboratory indicators of ESR and CRP (rSp=0.445; p=0.026), pain intensity according (VAS) (rSp=0.470; p=0.018). FM(FIRST) was positive in 50% of all patients, 52.9% - AS, 44.4% - RA. FM correlated with pain intensity (VAS) (rSp=0.699; p=0.001), EQ-5D (rSp=-0.659; p=0.001).

Conclusion. The majority of patients (69.3%) with immunoinflammatory diseases have mixed genesis of the pain, patients with RA are more affected by NP, AC - FM (with a predominance of the cognitive component). In the presence of NP and FM, patients have higher disease activity and lower quality of life.

P-11

Leaky gut-induced inflammation and amplification of pain due to unmentalized emotional distress can manifest as fibromyalgia: a case report

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Background. The etiology of fibromyalgia remains uncertain, but the co-occurrence of fibromyalgia with irritable bowel syndrome (IBS) and early life adversity are common.

Objective. Determine whether gastrointestinal factors in combination with early adversity may provide a plausible etiologic explanation for fibromyalgia.

Methods. We performed a literature review and case report.

Results. A geriatric patient presented to a psychiatric clinic with unspecified anxiety disorder, somatic symptom disorder, chronic pain in muscles and joints, and IBS. Medical records reveal over 20 medical hospitalizations and approximately 6,000 notes with no clear resolution. Traumas include primary caretaking for three younger siblings, a disabled mother prior to adolescence and death of an adult child in middle age. Employment history includes possible toxin exposures. Attempts to discuss childhood and adult traumas and related emotional distress resulted in increased perseverance on somatic concerns, specifically pain. The patient described therapy as "too intense" and instead opted to focus on physical issues. Small intestinal bacterial overgrowth leads to altered intestinal permeability (leaky gut) and inflammatory responses to foods that can trigger inflammation in muscles and joints.

Conclusion. Neglect and misattunement to needs in early development is associated with impaired emotional awareness, ineffective emotion regulation and impaired mentalization of social distress. In the context of pain due to inflammation, unmentalized distress can amplify nociceptive signals. Selective attention to physical pain reduces subjective emotional distress, which can be reinforcing. This combination is sufficient to explain the clinical appearance of fibromyalgia in some cases and provides new therapeutic options.

P-12

A multidimensional tool for the assessment of patients with juvenile fibromyalgia syndrome: the Juvenile Fibromyalgia Multidimensional Assessment Report (J-FiMAR)

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Objective. Juvenile fibromyalgia syndrome (JFM) is a chronic disabling condition. Validated pediatric outcome measures are currently lacking. The objective of the study is to validate a multidimensional tool for the assessment of patients with JFM.

Methods. We included JFM patients followed at our centre from 2019 to 2022. All patients were administered the J-FiMAR which includes numerical rating scales to measure the severity of JFM-related symptoms (pain, fatigue, sleep quality, depression, anxiety, cognitive impairment etc.) and self-report questionnaire to assess physical function and health-related quality of life. Convergent validity was tested by correlation analysis between the items of J-FiMAR and validated tools that measure the same constructs. Discriminant ability of J-FiMAR was evaluated by testing it in a group of 51 patients with active juvenile idiopathic arthritis (JIA).

Results. We included 51 patients (45 female; median age 16 years; median disease duration 1.8 years). All patients filled out the questionnaire shortly and considered it clear. Correlations between the J-FiMAR domains and validated measures of mood and sleep disorders were moderate (+0.4 r +0.6). JFM patients reported worse pain, fatigue and psychological distress than patients with JIA (p=0.05). VAS scores for pain, depression, anxiety, sleep disturbances and cognitive impairment were significantly lower

($p=0.001$) in JFS patients improved at follow-up compared to patients who did not improve according to the attending physician.

Conclusion. J-FiMAR was feasible and able to quantify global disease severity. Good results in terms of convergent validity, discriminant ability and responsiveness make J-FiMAR a promising outcome measure in JFM.

P-13

Factors driving disease severity and prognosis in juvenile fibromyalgia syndrome

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Background. Data regarding disease course and prognosis of Juvenile Fibromyalgia Syndrome (JFS) are scarce.

Objective. We aimed to identify symptoms driving disease severity and prognosis in JFS.

Methods. JFS patients followed at our center between 2019 and 2022 filled a multidimensional questionnaire at each visit, evaluating pain, fatigue, sleep quality, anxiety, depression, cognitive impairment and Patient Global assessment of disease severity (PGA) through 0–10 Visual Analogue Scales. Correlation and network analyses were performed to assess the relationship between symptoms, PGA and physician global assessment (PhGA). A mixed-effects logistic model was used to identify predictors of disease course.

Results. We included 51 patients (44 F; median age at onset 13.7 yrs; median disease duration 1.8 yrs). Patients were on regular physical activity in 83/194 (43%) follow-up (FU) visits and on medications in 70/194 (36%) visits. Pain and fatigue were the symptoms more strongly correlated with PGA ($r=0.68$, $r=0.62$, respectively) and PhGA ($r=0.52$, $r=0.53$, respectively). Networks analysis revealed fatigue as the most central symptom to predict other measures.

Twenty-nine out of 51 (56.8%) patients were classified as improved by treating physicians in at least one FU visit. Worse cognitive impairment at baseline predicted lower odds of improvement at follow-up (OR 0.81, 95% CL 0.68–0.97, $p=0.018$).

Conclusion. Pain and fatigue are the main determinants of disease severity. Cognitive impairment is a potential predictor of a poor outcome. Interventional studies are needed to determine whether targeting pain, fatigue and cognitive impairment can improve prognosis in JFS.

P-14

Chronic pain and depression in patients with fibromyalgia have strong correlations

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Fibromyalgia (FM) is one of most common chronic pain syndromes, affecting up to 5% of world population, is characterized of diffuse widespread body pain, with define clinical features, also triggers development of depression.

Depression severity in patients with fibromyalgia worsens severity of pain. The intensity of pain was assessed by visual analogue scale (VAS), Beck Depression Inventory (BDI) was applied to identify the depression and its levels in 151 patients with FM.

Test results on VAS show that in the total sample of patients with FM pain intensity in the range of 1-5 points (4.9 ± 0.25 , $M \pm SE$) was detected in 37.1%, 10.6 points (7.1 ± 1.25) -62.9% of patients.

BDI testing found that depression was detected in 86.8% of cases, where severity was distributed at mild (54.9%) and major (45.1%) levels.

It is well established that longer length of FM has a sharp decrease in the percentage of patients with no signs of depression, while patients with disease duration of more than 5 years were most prone to major depression.

These findings are consistent with the results of a number of authors: depressive disorders observed in approximately 90% of patients with FM.

Pain triggers development of depression in patients with chronic character of pain, time-course of disease shows certain pattern of increasing of severity of depression, and worsen long-term outcomes.

Patients with chronic pain must be necessarily evaluated for depression and successful management of the pain severity in those patients must include pharmacological treatment of depression too.

P-15

Registered cases of fibromyalgia syndrome and psychiatric and medical disease comorbidity (web-based)

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Due to the high burden and high cost of this disease on the patient and society, as well as the significant association of psychiatric disorders in patients with fibromyalgia, we decided to identify these patients in collaboration with psychiatrists and rheumatologists. Patient's demographic information has been recorded.

Age, Gender, Marriage status, Education, job, social, educational and interpersonal relationships, patient's financial situation, medical disease, psychiatric disorders, medications record in our registry system.

In this way, more accurate treatment plans can be made and society and health system costs will be reduced and the complications of the disease will be reduced. The recorded data also help physicians and researchers examine information about the manifestations and consequences of the disease in a large number of patients, and the results will be more generalizable to all patients with fibromyalgia and will not be limited to a small number of patients.

Objectives of the Registry:

1. Epidemiological study
2. Examining the rate of accompanying psychiatric disorders
3. Examining other accompanying physical diseases
4. Developing a plan to prevent and treat accompanying psychiatric disorders in order to improve the quality of life
5. to study the course and course of fibromyalgia and its relationship with psychiatric disorders
6. Calculating the years of disability and loss of useful life
7. Evaluate the effectiveness of intervention programs
8. Tracking patients after identifying the disease and controlling the treatment process.

List of Minimum Dataset (Variables):

Age / Gender / Marriage / Education / job / financial status/ insurance / Depression / Anxiety / Sleep Disorder / Sexual Disorder / Patient Personality / Quality of Life Based on Interviews and Questionnaires.

P-16

Viruses in fibromyalgia aetiology – new wisdom after the COVID-19 pandemic?

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Fibromyalgia (FM) has been defined in NRDP 2015 as a complex and contested syndrome, with prominent key symptoms: chronic widespread pain, problems with sleeping/strength recovering, physical exhaustion and cognitive difficulties (1). However, since the work of Garrity (2) and Goldenberg (3), it was suggested that many of the symptoms present in FM overlap with those of EM/CFS. This was also confirmed in 2000 by L. Aaron *et al.* (4) and very recently by the extensive meta-analysis of Ramirez-Morales and colleagues (5). Furthermore, several authors including Acheson (6), Buskila and Sarzi-Puttini (7) and Goldenberg (8) underlined epidemiological evidence for an association of FM/EM/CFS (considered here as a pathological “continuum”: F.E.C.) with previous viral infections or vaccinations. In 2010 – in the midst of diatribe over XMRV virus – I presented at the Chronic Fatigue Meeting in Italy a paper where I strongly criticized the hypothesized involvement of XMRV in these syndromes (9). The final review-manuscript was published in NMD in November 2012 after my prediction had been vindicated: there, I also reviewed previous viral-hunting and presented an alternative model for viral involvement (9). Today, over a decade later, a similar association is emerging after the COVID-19 pandemic caused by SARS-CoV-2 Coronavirus, as very recently reported by T. Wong (10) and by V. Versace (11). Rather than supporting a specific viral causation model – and has I have previously discussed (9) – these data suggest common pathways of immune-system (IS) and peripheral/central-nervous system (PNS/CNS) response to an overwhelming / potentially lethal infection (as MFV and SARS-CoV-2 are).

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P-17

Fatigue in patients with ankylosing spondylitis and fibromyalgia: associations with BDNF levelIryna Shapoval¹, Viktoriya Khomenko¹, Mykola Stanislavchuk¹

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Background. According to the last literature data, brain-derived neurotrophic factor (BDNF) closely related to the mechanisms of pain regulation and psychoemotional sphere, fatigue. But its role in patients with rheumatic diseases, like ankylosing spondylitis (AS) and fibromyalgia (FM), is not well understood. **Objective.** Our study aimed to determine associations between BDNF and fatigue in AS patients with FM.

Methods. 143 patients (81.8% male) with AS according to modified New York criteria included in the study. Mean age 42.1±11.3 years (M±SD). FM diagnosed by mACR2010 criteria. The severity of fatigue assessed by Multi-dimensional Assessment of Fatigue - MAF (Belza *et al.*, 1991). The BDNF level in plasma was determined at 8:00 and 20:00 by the ELISA and calculated the morning / evening ratio - BDNF index. The study was conducted according to bioethical standards. All data were analyzed using IBM SPSS 23. **Results.** FM was diagnosed in 49 (34.3%) patients and in 89% of all patients noted fatigue. We found statistically significant correlations of fatigue with morning (r=0.201, p=0.05), evening BDNF levels (r=0.508, p=0.01) and BDNF index (r=0.459, p=0.01).

For a deeper analysis, we divided AS patients into 2 groups depending on BDNF index: with “Low” 0.95 and “High” 0.95. “Low” BDNF index was determined in 52 AS patients (36.4%). In group with “High BDNF index” mean scores (M±SD) of MAF were - 26.4±7.76 and in group with “Low BDNF index” - 34.9±8.47 (p=0.01). In group with “Low BDNF index” we met FM in 75% patients (39 persons) and in group with “High BDNF index” only in 11% patients (10 persons).

Conclusion. “Low” BDNF index is associated with fatigue and FM in AS patients.

P-18

Fibromyalgia descriptions in ancient Ayurveda treatises. Ayurveda could provide safe, authentic affective personalized holistic solutions

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Background. Ayurveda, the futuristic Indian medicine has stood the test of time. Charaka Samhita one of the most authentic medical texts describes Alzheimer’s diseases, Multiple Sclerosis and many other chronic neurological degenerative autoimmune conditions and in the same chapter Fibromyalgia has been described. Fibromyalgia is termed as Samanavrttaapana Vatavyadhi. It is a chronic neurological relapsing remitting condition of pain. The hallmarks described include pain in the flanks, irritable bowel syndrome, pain in the chest, lower abdomen, symptoms are unprovoked, unanticipated-aggravating and relieving factors. This Ayurveda describing a similar condition of FM has been highlighted to showcase the first enumeration of the condition. **Objective.** Neurological conditions are termed as Vatavyadhi and a very elaborate understanding of etiological factors, relapses, remissions, triggering and mitigating factors based on Ayurveda perception has been enumerated, Aetiology, symptoms, pathology, manifestation, complications unique. Cases diagnosed based on the Ayurveda principles and the present-day concepts but treated on Ayurveda principles have been compared at all levels. **Methods.** Preventive and curative principles and practices have been in vogue since many centuries and case study which has significant results have been highlighted. **Results.** Relapses and intensity has marked reduced. Ayurveda life style, yoga lifestyle, simple medications which are personalized and precise had been prescribed which ensured better life style, helped increase in workdays and decreased fatigue. **Conclusion.** Ayurveda could benefit more patients suffering from FM if principles and practices could be adopted in large sample size. Climatic challenges, personalized food and life style habits could play a significant role in the management of FM.

P-19

The FM-HI: Development and validation of a novel fibromyalgia outcome measure

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Background. In preparation for upcoming clinical trials in fibromyalgia (FM), there is a need for valid, reliable, and sensitive, patient-reported outcome measures that are capable of detecting clinically relevant changes in disease burden over time and satisfying FDA criteria for use in therapeutic trials and drug labeling claims.

Objective. We have developed and validated the FM-HI (Fibromyalgia-Health Index) for use in FM therapeutic trials and clinical monitoring.

Methods. We conducted semi-structured qualitative interviews with individuals with FM to identify symptoms of potential importance in FM. Next, we conducted a cross-sectional study to determine the symptoms of greatest prevalence and impact in FM. We selected questions for the FM-HI based on their high relevance and potential responsiveness to therapeutic intervention. We used factor analysis to group similar symptoms into subscales representing symptomatic themes of FM health. We performed beta testing, known groups testing, and test-retest reliability assessments to optimize instrument clarity, usability, meaningfulness, responsiveness, and reliability.

Results. Fifteen individuals with FM participated in qualitative interviews and a total of 1,044 participants completed the cross-sectional study. Validation testing found the FM Health-Index and its subscales to be highly relevant, reliable, and capable of distinguishing between individuals with differing levels of disease burden. The final FM-HI contains 12 subscales that comprehensively measure patient-reported disease burden in FM.

Conclusion. The FM-HI provide researchers and clinicians with a highly sensitive and reliable mechanism to measure relevant changes in how patients feel and function over time or in response to therapeutic intervention.

Complex CNS

P-20

Event-related potentials and oscillations during an emotional stroop task in patients with fibromyalgia syndrome

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Background. Fibromyalgia syndrome (FMS) is a chronic condition of widespread pain accompanied by symptoms like depression, fatigue, sleep disturbance and cognitive impairments. In addition to central-nervous pain sensitization, emotional dysregulation may be involved in the pathogenesis of FMS.

Objective. This study investigated emotional influences on cognitive processing in FMS. Therefore, event-related potentials (ERPs) and theta oscillations were recorded during an emotional Stroop task in 36 FMS patients and 35 pain-free controls.

Methods. In the task participants had to decide whether the colors of positive, negative, and neutral adjectives accorded with color words presented in black. Comorbid psychiatric disorders were also assessed.

Results. FMS patients had larger P3 amplitudes, longer P3 latencies and greater theta power than controls, independent of the emotional content of the words. In patients, but not in controls, negative words were associated with a larger late positive component (LPC) amplitude than positive words. No group differences arose for the P1, early posterior negativity and N4. Reaction times (RTs) were longer in FMS patients than controls, independent of emotional word content. Comorbid depression and anxiety were unrelated to EEG parameters and RTs.

Conclusion. The findings pertaining to P3 and theta oscillations may indicate greater cognitive effort and attentional mobilization in FMS, needed to overcome the reduction of attentional resources resulting from central-nervous pain sensitization. Though RTs do not support attentional bias in FMS, the emotional modulation of the LPC amplitude may reflect preferential central-nervous processing of negative information, which contributes to enhancement of pain and affective symptoms in the disorder.

Neuro-biological underpinnings of fibromyalgia and centralized pain**P-21****A new artificial intelligence drug repurposing approach for fibromyalgia**

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Background. Fibromyalgia (FMS) is a complex syndrome with still unknown aetiopathogenesis and an intricate polysymptomatology. Consequently, there is still a tremendous lack of efficacious therapies. In the last years we implemented, with promising results, an algorithm that assigns a probability score to drug-receptor pairs. In our proof-of-concept study, we worked on another disease (anxiety) to set up the method for drug repurposing.

Objective. The main objective of the present work is to implement an artificial intelligence-based drug repurposing approach applied on the proteins putatively involved in FMS.

Methods. DisGeNET database was used to retrieve FMS related proteins. Networks were generated and topologically analysed by Cytoscape. The implemented algorithm to assign a probability score to drug-receptor pairs was written in Python (drugs: retrieved by DrugCentral; receptors: proteins of the FMS network, structure predicted by AlphaFold).

Results. By retrieving available information about proteins related to FMS (143), we built a protein network that allowed us to visualize the interactions among proteins variously associated to the disease. Surprisingly, the network had more edges than expected (p1e-16). Moreover, we analysed the topology of the network to discriminate the most important nodes, *i.e.*, the probable central proteins in the etiopathogenesis. ALB and BDNF resulted to have the highest betweenness centrality.

Conclusion. The high connectivity of the FMS network suggests that proteins so far associated to the disease may have a role in the same biological pathways/complexes. The central nodes are the most interesting druggable targets. Pair scoring is ongoing.

P-22**Brain structure in pain processing regions of fibromyalgia patients relates to peripheral markers of small fiber neuropathy**

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Background. Fibromyalgia syndrome (FMS) is frequently investigated using neuroimaging methods to demonstrate structural brain changes in patients relative to healthy people. However, findings across studies are extremely heterogeneous. In recent years, a new focus on peripheral nervous system structure and function points to a potentially important role for small fiber neuropathy (SFN) in FMS. Despite this, no research has yet considered brain structure in tandem with peripheral markers of SFN.

Methods. 22 patients with FMS underwent a deep central and peripheral phenotyping regime including structural MRI scans to consider brain anatomy, skin biopsy and corneal confocal microscopy (CCM). Automated processing of retinal images quantified peripheral markers of SFN including Ocular Surface Disease Index (OSDI), and corneal nerve length and branch density. Regional grey matter density and cortical thickness were evaluated using the Computational Anatomical Toolbox in SPM12.

Results. Initial findings indicate a correlation between corneal nerve branch density (a marker of degenerative and regenerative activity) and grey matter density in key pain processing regions of the brain including insula and anterior/mid-cingulate cortices.

Conclusion. For the first time, our findings indicate a relationship between structural integrity of the peripheral nervous system with key pain processing brain regions identified in previous research of FMS. As a cross sectional study, causality cannot be inferred, but we hypothesise that brain structural changes could occur as a result of SFN in FMS. We argue for a more holistic approach considering both central and peripheral nervous system structure and function to improve understanding of FMS pathophysiology.

P-23**Self-reported long-term pain of unclear origin and psychosocial associations**

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Background. Many studies indicate that a central sensitisation to pain in fibromyalgia syndrome, a pain of unclear origin, could be associated with childhood maltreatment and insecure attachment.

Methods. A cross-sectional study with representative samples of the adult population in the Czech Republic (n=1800, mean age 46.6, 48.7% of men) and Slovak Republic (n=1018, mean age 46.24 years, 48.7% men) collected data on health status (questions on selected long-term diseases including the pain of unclear origin and the SF-8 Health Survey), childhood maltreatment (The Childhood Trauma Questionnaire, CTQ), and attachment (The Experienced Close Relationship-Revised, ECR-R). Participants were divided into three groups: 1. subjectively healthy (n=781), 2. with long-term pain of unclear origin (n=165), and 3. with other long-term diseases (n=1872). Results were analysed by the non-parametric Kruskal-Wallis test and **multinomial logistic regression model, adjusted for gender and age.**

Results. Participants with long-term pain of unclear origin were 54.5 % men, 52 % were older than 60 years and 18.2% were widowed. They had higher attachment anxiety and avoidance ($p=0.001$) and scored significantly worse in all subscales of the health survey ($p=0.001$). Emotional and physical abuse, and emotional and physical neglect were strong predictors for the pain of unclear origin.

Conclusion. Our findings are pointing to associations between childhood maltreatment, attachment insecurity and pain of unclear origin. Even if this study has not assessed the clinical diagnosis of fibromyalgia, we assume that many of the respondents reporting long-term pain of unclear origin would fulfil the clinical criteria of fibromyalgia.

P-24**Involvement of sex hormones and glucocorticoids in a thalamo-cortical loop model of fibromyalgia pathogenesis**

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Background. Fibromyalgia (FM) is a puzzling central disorder characterized by chronic pain, sleep disruption, fatigue, and other symptoms. FM has a marked female prevalence and is correlated with stress, suggesting a role for sex hormones and glucocorticoids. Early FM model. We have previously proposed a model of FM chronic pain based on a thalamocortical loop system, fitting various FM clinical and neuroimaging data. The loop system can become a bistable switch upon a weakening of GABAergic transmission between the thalamic reticular and ventroposterolateral nuclei. Hence, FM pathophysiological transition would be driven by factors that induce an unbalance in the ratio between GABA and glutamate. Advanced FM model. The alleged roles of hormones and neurotransmitters fit perfectly together, allowing to realize a complete model of the disease spanning from external stimuli to symptoms. All sex hormones have been found to modulate neurotransmitters, including GABA and glutamate. Most investigated is GABA strengthening exerted by a moderate increase of allopregnanolone, a progesterone neurosteroid derivative. In contrast, cortisol is detrimental on GABA and strengthens glutamate. These pieces of evidence can be implemented within a comprehensive model, because the HPG and HPA axes interplay in a double-negative loop system, potentially acting as a bistable switch.

Conclusion. Especially in women, strong stressful stimuli, combined with progesterone lowering phases, could switch the endocrine loop to high-cholesterol/low-allopregnanolone steady state, thereby converting the thalamo-cortical neural loop to bistability, and eventually making it fall into a high-excitation status, resulting in the chronic pain and allied central disorders of FM syndrome.

P-25

Fibromyalgia, attention deficit hyperactivity disorder, obstructive sleep apnea and pain perception

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Background. Fibromyalgia (FM) is often comorbid with and exacerbated by Obstructive Sleep Apnea (OSA). Attention Deficit Hyperactivity Disorder (ADHD) is a neurodevelopmental disorder thought to be prevalent among children and adults. Understanding the relationship between FM, OSA, ADHD and pain perception is important.

Objective. Co-occurrence of ADHD and FM was assessed, as well as the burden of pain associated with FM, OSA, and co-morbid ADHD.

Methods. This pilot study of 38 patients with FM and comorbid OSA examined if ADHD was present and correlated with pain perception. Adult ADHD Self-Report Scale (ASRS-v1.1) Symptom Checklist Questionnaire 1 and Short-Form McGill pain questionnaire (SF-MPQ)2 were administered. Descriptive statistics were utilized to describe patient demographics and summary scores.

Results. FM n=38, males n=2, females n=36. Mean age: 60.60. FM + ASRS-v1.1 positive screen: n=18 (47%), age: 60.27. Reported symptoms present during childhood age n=10 (26%). FM + ASRS-v1.1 negative screen: n=20 (52%), age: 60.94. Overall SF-MPQ in ADHD positive: 26.56 (n=18). Overall SF-MPQ in ADHD negative: 19.10 (n=20). There was a significant difference ($p=0.045$) in pain perception between patients with ADHD and FM compared to those with FM alone.

Conclusion. Comorbidity of ADHD (47%) suggests attention deficits are common in patients with FM and comorbid OSA. Higher pain perception in ADHD positive patients suggests attention problems may enhance perceived pain in FM.

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P-26

The correlation between pain and chosen cognitive functions-attention and ability of learning

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Background. Fibromyalgia (FM) is a psychosomatic disorder, which has a complex etiology. Due to the lack of scientific consensus on the origins of FM, the varied clinical presentations and normal inflammatory markers in the body, FM is considered difficult to diagnose and is often diagnosed less frequently than its occurrence. Several publications report individuals with FM manifest cognitive dysfunction such as memory impairment.

Objective. The aim of the study was to evaluate attention and learning processes in patients with primary fibromyalgia syndrome (PFS).

Methods. The study recruited 60 subjects including 30 PFS patients and a reference group of 30 patients with lumbar degenerative disc disease (DDD). Respondents completed Wisconsin Card Sorting Test (WCST), 10-word learning task, and Benton's Visual Retention Test. They were also administered Beck Depression Inventory (BDI) to evaluate depression and Visual Analogue Scale for self-report of pain to explore the moderating effect of depression and pain on cognitive performance.

Results. FM participants obtained significantly poorer results ($p=0.05$) in Benton test than controls indicating poorer visual memory performance in FM. Pain intensity caused (VAS SCALE) significant moderating effect on the efficiency of learning and memory processes but the effect of the severity of depressive symptoms on the number of errors in memory tests could not be indicated.

Conclusion. The results of the study reiterate that pain in FM patients should be treated by a combination of pharmacological and non-pharmacological methods.

Treatment of fibromyalgia

P-27

Efficacy of physiotherapy treatment in medium and long term in adults with fibromyalgia: an umbrella of systematic reviews

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Objective. To synthesize available knowledge about physiotherapy treatment in medium and long term in adults with fibromyalgia.

Methods. Three independent investigators selected systematic reviews about non-pharmacological treatment in medium and long-term in patients with fibromyalgia. Searches were performed on six main electronic databases and the risk of bias of included systematic reviews was assessed using the PRISMA checklist.

Results. The initial search identified 1220 studies, subsequently a total of 32 articles were included. The most used non-pharmacological treatment in the added systematic reviews was therapeutic exercise. Findings from these systematic reviews suggested that therapeutic physical exercise (such as aerobic, water exercise, Tai Chi, Qi Gong, Pilates, Yoga, or stretching) results in improvement in variables analyzed using the visual analogue scale and Fibromyalgia Impact Questionnaire score. Regarding the internal quality of the documents, the values analyzed with PRISMA range from 11 to 25, with an average score of 18.5. Other therapies such as repetitive transcranial magnetic stimulation or transcranial direct current stimulation also showed an improvement in pain and functionality with respect to the scores of the questionnaires used.

Conclusion. Therapeutic physical exercise and non-invasive transcranial stimulation are the two main treatments for fibromyalgia that are showing excellent results according to the outcomes analyzed. However, studies of greater methodological rigor are needed, which make it possible to carry out high-quality clinical studies and systematic reviews that can create recommendations to correctly guide clinical practice in rehabilitation.

P-28

Group therapy for fibromyalgia: a randomized controlled trial of mindfulness-based therapy versus cognitive-behavioral therapy

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Background. Fibromyalgia (FM) is a chronic pain disorder, highly comorbid with depression, stress, and anxiety. While mental health interventions for FM have been studied, only few studies have compared the effectiveness of different psychotherapies.

Objective. We aimed to examine the effectiveness of group cognitive-behavioral therapy (CBT) and group mindfulness-based stress reduction (MBSR) in reducing psychological and physical distress among FM patients.

Methods. The study is a randomized controlled trial (RCT) including Ninety-three (93) FM patients (mean age=47.25, SD=12.4) recruited from one of Israel's largest community healthcare providers. Patients were randomly assigned to 3 conditions: (1) Group CBT (n=32), (2) MBSR (n=29), (3) Waitlist control group, subsequently assigned to treatment (n=32). Participants completed self-report questionnaires assessing FM symptoms (FIQR), Health related quality of life (HRQOL) and Major depression (PHQ-9), at 3 assessments: pre- and post- treatment, and 4 months after treatment.

Results. Compared to the WL and CBT, the MBSR group showed greater improvements in Fibromyalgia symptoms. Compared to the WL, the MBSR group showed greater improvements in MDD and HrQOL. CBT participants showed improvements in Fibromyalgia symptoms and Physical QOL between pre- and post-treatment.

Conclusion. These results reveal the significant therapeutic potential of MBSR for Fibromyalgia patients, above and beyond CBT. The mind-body emphasis which is inherent in MBSR may render this approach particularly suitable for FM.

P-29

Feldenkrais awareness through movement intervention for fibromyalgia syndrome: a proof-of concept study

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Background. The Feldenkrais Method is a form of awareness through movement (ATM) which aims at increasing awareness about spatial and kinesthetic relationships among body segments and the environment thought verbally guided movements (1). Fibromyalgia syndrome (FM) is a form of chronic widespread pain associated to a variety of ancillary symptoms, among which fatigue, sleep disturbances and regional pain syndromes are preponderant. Lately, increasingly more attention has been drawn on mind-body interventions and meditative movement therapies for FM treatment (2). ATM application for chronic pain has been promising but with low quality studies (3,4).

Objective. The aim of this study was to explore the effectiveness of ATM for FM patients after 4 months of ATM activity; in particular, the proof-of-concept design aims at determining the domains for which an ATM-based intervention may be effective for FM patients.

Methods. This is a proof-of-concept, observational, non-controlled prospective study which lasted 6 months. Participants were recruited by the Italian Fibromyalgia Syndrome Association (AISFOdv), a non-profit patient organization, through social media advertising. After signing the informed consent, they were divided into eleven groups of eleven/twelve patients each. Two Feldenkrais teachers were assigned to each group. All patients attended an ATM course lasting 15 lessons, with a lesson every h long (from January to May, 2021). The sessions were entirely virtual platform-based and live. Clinimetric tests and patient-reported outcome tests were administered at baseline and at the end of the intervention.

Results. One hundred and twenty-eight FM patients (mean age 54 years old, 2% males) participated in the study. A statistically significant improvement was found in FM-specific measures (Polysymptomatic Distress Scale, PDS) ($p=0.003$) and the Pain Catastrophization Scale (PCS) ($p=0.020$); coherently, the amelioration in the Revised Fibromyalgia Impact Questionnaire (FIQR) almost reached statistical significance ($p=0.08$). The logistic regression analysis found a correlation between PDS, fatigue and anxiety measures; PCS, years from diagnosis and anxiety.

Conclusion. In conclusion, ATM could improve FM-specific measures and pain-related catastrophizing. Improving awareness about one's own body and movements through ATM sessions may have helped FM patients to improve their cognitive attitude towards their pain condition, embracing a more positive, hence less catastrophizing attitude; furthermore, ATM could benefit FM patients because of its induction of muscular relaxation (5). Further studies are needed to identify FM subgroups in order to find personalized targets that can be used to guide treatments.

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P-30

Pharmakon or the art that heals: trans-disciplinary artistic transformative workshops for fibromyalgia syndrome

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Background. Fibromyalgia syndrome (FMS) is a widespread chronic pain syndrome with many associated symptoms. It is frequently related to a traumatic event (1), strong and of short duration, or slight but protracted over time. A multidisciplinary therapeutic approach is recommended by international guidelines. The transformative experience (TE) allows for a profound and immediate change that differs from linear and gradual psychological change; this helps create novel responses to the same initial thoughts and actions, thereby breaking the maladaptive emotional/behavioral loop elicited by chronic stress and trauma (2), creating a sort of "virtuous" cycle, adaptive rather than maladaptive and long-lasting. In this study, TE was specifically elicited through transformative art (TA), an intrinsically transdisciplinary tool, in different ways in the three arms of the study.

Objective. Validation of the efficacy (in terms of quality of life and sleep, self-esteem, self-efficacy) of transdisciplinary artistic-transformative pathways in patients with FMS.

Methods. Prospective observational study lasting 8 months (February-October, 2021), in which the effectiveness of three different TA workshops in patients with FMS was evaluated: in group 1 participants were encouraged to review their autobiography and illness in a humorous sense; in group 2 participants were guided to express their own realities of chronically ill patients in poetry; group 3 was based on the guided narration of works of art according to visual thinking strategies integrated with the principles of narrative medicine. Patients were divided into the three laboratories according to their preference. Tests were administered at baseline and post-workshop. The activities took place entirely online.

Results. 109 FM patients completed the study (n=3 males, mean age 52.9, mean years from diagnosis 11.2 [SD 8.6]). No differences were found among the three groups at baseline in terms of clinimetric variables. Data analysis made by a Wilcoxon non-parametric test (WNPT) of the three groups in conjunction showed a statistically significant improvement of the Pittsburgh Sleep Quality Index (PSQI) ($p<0.05$), Response to Stressful Experiences Scale (RSES) ($p<0.05$), World Health Organization- Five Well-Being Index (WHO-5) ($p<0.001$) and Global Health scale (GH) ($p<0.05$). No significant difference was found for The Mindful Attention Awareness Scale (MAAS) ($p=0.2663$). A WPNT was performed to compare baseline and final results of the three groups separately. The best performance was seen in Group 1, since patients ameliorated in almost all parameters: PSQI ($p<0.05$), GH ($p<0.05$), SAP dimension 1 ($p<0.05$), 2 ($p<0.05$) and 4 ($p<0.05$), WHO-5 ($p=0.0013$), MAAS ($p=0.895$), RSES ($p=0.0673$) and SAP dimension 3 ($p=0.0573$) resulted nonsignificant, although very close to significance. Sleep ($p<0.05$) and the 3rd dimension of SAP ($p<0.05$) improved in patients of Group 2; whilst self-esteem ($p<0.05$) and WHO-5 ($p<0.05$) did in Group 3.

Conclusion. Our research shows that art, experienced as TA, leads to significant improvements of the psychophysical condition of FMS patients. TA can be seen as a crucial mediator for overcoming the trauma/stressors, probably through the generation of "pivotal mental states" (PIMS), defined as a "hyper-plastic state aiding rapid and deep learning that can mediate psychological transformation" (3).

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P-31

Acquired torticollis in a fibromyalgia patient: a case report

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Background. Torticollis is tonic posturing of the head in a rotated, twisted, or abnormally flexed or extended position.1 Fibromyalgia patient who did not move their neck or shoulders for long time tend to report more severe neck symptoms. Till now, no published literature has been there correlating torticollis and fibromyalgia.

Objective. To report acquired torticollis entity in a diagnosed case of fibromyalgia patient.

Case brief. A fibromyalgia patient with neck pain (VAS=80) had postural tilt on right side with tender right side sternocleidomastoid with limited neck mobility. USG guided trigger point injection of right sternocleidomastoid follow by physiotherapy and medication had increased neck mobility.

Discussion. Here, the fibromyalgia patient had abnormal posturing of neck causing contraction of sternocleidomastoid of right side with trigger areas. Torticollis is a marked by of the painful cervical musculature dystonia resulting in unwanted sustained head protrusions and neck tilt on affected side with severely restricted neck mobility resulting in diffuse pain located in the neck and shoulder region seen in 70-80% cases. Sternocleidomastoid muscle is involved in 75 percent cases.1

Conclusion. Thorough history and examinations are the key to the diagnosis and treatment of associated myofascial pain in a case a fibromyalgia. Myofascial trigger point injection along with adjunctive medication and stretching exercise can maximize the pain relief and range of motion. It can increase the compliance of patient for further management of fibromyalgia.

P-32

Efficacy and safety of TNX-102 SL (sublingual cyclobenzaprine) for the treatment of fibromyalgia: results from the randomized, placebo-controlled RELIEF trial

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Background. Fibromyalgia is a chronic pain disorder that results from amplified sensory and pain signaling within the CNS.

Objective. To evaluate the efficacy and safety of TNX-102 SL*, a once-nightly sublingual formulation of cyclobenzaprine, in reducing pain in patients with fibromyalgia.

Methods. RELIEF was a double-blind, randomized, placebo-controlled trial (n=503). Patients received TNX-102 SL 2.8 mg for 2 weeks, followed by 5.6 mg for 12 weeks (n=248) or matching placebo (n=255). The primary endpoint was change from baseline at week 14 in weekly average of daily pain scores. Secondary endpoints included Patient Global Impression of Change (PGIC) scores, Fibromyalgia Impact Questionnaire Revised (FIQR) scores, PROMIS sleep disturbance and fatigue scores, and daily sleep quality. Safety was assessed by adverse events (AEs).

Results. Reduction in daily pain from baseline at week 14 was significantly greater with TNX-102 SL (LS mean change [95% CI], -1.9 [-2.1 to -1.7]) vs. placebo (-1.5 [-1.7 to -1.3]; $p=0.010$). TNX-102 SL was not associated with significant improvement in PGIC at week 14 but was associated with improvements in FIQR, PROMIS, and daily sleep quality. 59.7% of patients receiving TNX-102 SL and 46.3% receiving placebo reported treatment-emergent AEs; the most common were oral hypoesthesia (17.3% with TNX-102 SL vs. 0.4% with placebo), oral paresthesia (5.6% vs. 0.4%, respectively), and product taste abnormal (4.4% vs. 0.4%, respectively).

Conclusion. Treatment with TNX-102 SL was associated with significant reductions in daily pain and was safe and well tolerated.

*TNX-102 SL has not been approved for any indication.

P-33

Conniving of prophetic variables of medical importance and their impending role to develop fibromyalgia

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Background. Fibromyalgia (FM) is a widespread syndrome that lack any evident reason and may be characterized with the existence of chronic pain of unknown etiology. Still the well-defined etiology and theranostic approach tranquilly awaiting to diagnose and most importantly its therapeutic treatment.

Objective. The prime objective of the current study was to determine the key variables of diagnostic and theranostic importance to treat fibromyalgia. **Methods.** Serum levels of hundred fibromyalgia subjects of interleukins, matrix metalloproteases, tumor necrosis factor were assayed by their respective commercially available ELISA kits. Contingency table was drawn upon the recorded data to rule out sensitivity, specificity, accuracy and odds ratio at 95% CI.

Results. The results of the present study shows that IL-1, IL-1RA, MMP-2 and TNF- α stands to be most sensitive (SN) and specific (SP) markers with SN-SP of (73%-95%, 67%-93%, 67%-88%, 53%-76%) respectively.

Conclusion. Findings of the current study entitles the importance of IL-1, IL-1RA, TNF- α , IL-18 and MMP-2 shows maximum accuracy along with higher sensitive and specific range in fibromyalgia. Higher values of odds ratio determines that IL-1, IL-1RA, TNF- α , IL-18 and MMP-2 are more specific and sensitive for fibromyalgia. Thus, their early detection could have significant importance in ruling out the disease condition. Maximum accuracy along with higher sensitive and specific range of the said variables may have medical and theranostic importance to treat fibromyalgia.

P-34

Patients with moderate fibromyalgia syndrome had improved functional status after receiving remote approach based external myofascial mobilization: a retrospective analysis

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Objective. Fibromyalgia (FM) is a chronic pain syndrome characterized by a large variety of symptoms. The purpose of this study is to evaluate the outcome of a four-week Remote approach based external myofascial mobilization (RAEMM) program based on myofascial connectivity in the management of patients with fibromyalgia syndrome.

Methods. retrospective chart review of patients with a diagnosis of fibromyalgia who underwent RAEMM therapy between March 2020 and April 2022 was organized for this analysis. The outcomes at a follow up visit at 6 months were also extracted. The functional status, twenty-four-hour pain status quality of life and sleep were analyzed at the baseline, after completion the program and at 6 months.

Results. The data from 19 moderately affected female fibromyalgia patients who completed the RAEMM therapy and the follow up session at 6 months were included in the analysis. The mean (range) age of patients was 46 (28-62) years. The mean (SD) FIQ score at initial evaluation was 64.8 (9.3) and decreased to 26.7 (6.4) at the post test and remained largely unchanged at 6-month follow-up (28.5 \pm 8.3), indicating a robust treatment response. Analysis of the 24-hour pain behavior also revealed significant improvement in pain ($p=0.001$) with a retaining of effect at 6 months follow-up.

Conclusion. A RAEMM approach based on fascial connectivity led to significant symptom improvement in all the studied patients. The relative retention of effects found in the pain and the quality-of-life scales at the follow-up was promising finding. RAEMM may be an effective treatment option for fibromyalgic patients with moderate symptoms. Future high-quality studies with control groups are needed to confirm the present findings and to identify the effects on chronicity, durability, and long-term outcomes.

P-35

Efficacy of transcutaneous vagus nerve stimulation implementations in fibromyalgiaAlper Perçin¹, Ali Veysel Özden²¹Physiotherapy and Rehabilitation, Iğdır University, Türkiye; ²Physiotherapy and Rehabilitation, Bahçeşehir University, Türkiye

Background. Fibromyalgia is a disease characterized by autonomic nervous system disorder. The ineffectiveness of the methods used to suppress symptoms in the long term led to the search for other treatment methods. Studies have shown that sympathetic activity dominance was observed in patients with fibromyalgia when heart rate variability (HRV) was measured. This situation has revealed the need to review autonomic modulation methods to stimulate parasympathetic nervous system activity. Transcutaneous auricular vagus nerve stimulation (tVNS) comes to the fore in this period due to the lack of side effects and the low cost of the application.

Objective. The aim of this study is to review the studies conducted with patients diagnosed with fibromyalgia who underwent tVNS to compile the results and to have an idea about the effectiveness of the treatment.

Methods. In the studies conducted on the Pubmed database, randomized controlled studies conducted in patients diagnosed with fibromyalgia between 2011 and 2020 were examined and four studies that were considered suitable for our study were included.

Results. Although there was no significant decrease in the severity of symptoms experienced by the patients in the application of tVNS applied to individuals with fibromyalgia, a significant decrease was observed in the sub-parameters indicating sympathetic activity when the HRV parameters were examined.

Conclusion. Achieving standardization in tVNS application seems to be a more effective way to increase treatment efficiency. In fibromyalgia syndrome, in addition to other physiotherapy modalities, tVNS application may help increase parasympathetic activity dominance and suppress symptoms together with autonomic modulation.

P-36

Fibromyalgia patients with the highest stage of chronification. therapy options and outcome - evidence from GermanyTobias Romeyke¹*Institute for Management and Economics in Health Care, University of Health Sciences, Medical Informatics and Technology, Austria*

Background. Fibromyalgia (FM) causes pain in different parts of the body. In addition to headaches, gastrointestinal complaints and concentration problems, patients can also develop mental complaints such as inner restlessness, feelings of anxiety, despondency and even depression. Due to the complex nature of the disease, it is difficult to find suitable therapies. The multimodal rheumatological complex treatment (MRC, OPS 8-983) is an acute inpatient care concept that is used in the German health care system by highly specialized clinics. It is used to treat acute exacerbated pain and functional limitations that can be caused by soft-tissue rheumatic diseases.

Objective. The examination of therapy results after performing MRC. The patient collective included patients with confirmed FM and the highest degree of pain chronification (Gerbershagen stage III).

Methods. 233 FM patients were treated in a specialized clinic (Waldhausklinik Deuringen) using MRC. Health-related quality of life was assessed at admission and discharge using the Nottingham Health Profile (NHP). Pain-related disability using the Pain Disability Index (PDI), physical functional limitations using the FFbH and general complaints using the v. Zerssen Score.

Results. The MRC took an average of 16.13 days to complete. PDI decreased from 43.6 to 35.55 points, FFbH improved from 53.11 to 57.64% and the general complaints were reduced from 41.43 to 34.68 points. Using MRC improved quality of life in all dimensions of the NHP.

Conclusion. Inpatient multimodal therapies with a high therapy density and defined therapy content can help FM patients with the highest degree of chronicity. They should be further expanded in the international health systems due to their evidence.

P-37

The effect of blood flow restricted aerobic exercise training on pain, functional status, quality of life and hormonal response to exercise in fibromyalgia patientsMert Zure¹, Mahir Topaloglu², Sina Arman³, Aysegul Ketenci²¹Physical Medicine and Rehabilitation, University of Health Science, Kanuni Sultan Suleyman Research and Training Hospital, Türkiye; ²Physical Medicine and Rehabilitation, Koc University Faculty of Medicine, Koc University Hospital, Türkiye; ³Physical Medicine and Rehabilitation, Istanbul University Istanbul Faculty of Medicine, Türkiye

Objective. The aim of the study is to investigate the effects of aerobic exercise program with blood flow restriction on pain, functional status, quality of life and hormonal response to exercise in patients diagnosed with fibromyalgia.

Methods. 46 female patients with fibromyalgia, aged 24-55 years, were included in this prospective, randomized and controlled study. Participants were randomized into two groups as the blood flow restricted aerobic exercise group (n=23) and the control group (n=23). The patients in both groups underwent supervised aerobic exercise four times a week for six weeks. Blood flow restriction was provided with elastic bandages at the groin level during exercise, while the real blood flow restriction protocol was applied to the experimental group, sham blood flow restriction was applied to the control group in the same time and number of sessions. The Fibromyalgia Impact Questionnaire (FIQ), which addresses the severity of the disease from many aspects, was used as the primary outcome measure. As a secondary outcome criterion; Central Sensitization Index (CSI), Beck Depression Scale (BDS), Pain Assessment with Visual Analogue Scale (VAS Pain), Chronic Pain Acceptance Questionnaire-8 (CPAQ-8), 24-hour urine VMA and 5-HIAA levels were used. Measurements were repeated before the intervention, immediately after the 6-week intervention and at the third month after the intervention.

Results. The mean age of the patients was 43.2±7.2 years. In the initial evaluation, the two groups were found to be homogeneous in terms of demographic and clinical parameters. Compared to the control group, a significant decrease in FIQ values was detected in the blood flow restricted exercise group ($p=0.001$), a significant decrease in CSI, BDI values, and a significant increase in 24-hour urine VMA and 5-HIAA levels ($p=0.001$) were also detected. Although there was a significant decrease in the VAS Pain value and a significant increase in the CPAQ-8 value, there was no significant difference between the groups concerning these outcomes.

Conclusion. In this study, it was found that the functioning, central sensitization, mood improved and catecholamine-serotonin levels increased with the aerobic exercise program with blood flow restriction applied in women diagnosed with fibromyalgia. In addition, with this treatment, reduction in pain and increase in pain acceptance was achieved.

“Transparent pain”: How society deals with fibromyalgia

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“Transparent illness” - a sense of otherness and human dignityLiraz Cohen-Biton¹, Rachel Nissanholtz-Gannot², Dan Buskila³¹Faculty of Social Work, Ashkelon Academic College, Israel; ²Department of Internal Medicine Health, Ariel University, Israel; ³Department of Internal Medicine Health, Ben-Gurion University of the Negev, Israel

Fibromyalgia is characterized by diffused Musculoskeletal pain and intense tenderness over many places in the body combined with fatigue. The disease severely impairs the level of professional, social and family functioning of those who suffer from it. It is a transparent disease. In other words, outwardly it is invisible. There are over 200 transparent diseases such as endometriosis and CFS where 80% of the patients are women. The term “transparent disease” is not a medical term as it bears a medical diagnosis. However, patients have to prove socially that they have a disability, therefore, it is a social phenomenon. The patients undergo a long and difficult diagnostic process and suffer from unexpected outbursts of pain. In these diseases there is no identity of “I am sick” or “I am not sick” as the encounter between health and sickness is undistinguished. Moreover, for the general public these diseases and the women who suffer from them are transparent hence emerge the power relations with the medical system. We sought to examine the perceptions of fibromyalgia patients in relation to their disease. We interviewed patients diagnosed with fibromyalgia who underwent fibrotherapy treatment program for 30 weeks. Fibrotherapy is a holistic body-mind approach designed to empower the patient’s ability to accept the disease and find the right way to manage it. The difficulty in identifying and diagnosing the disease and the social perception in relation to being a fibromyalgia disease, is a common phenomenon: “Only after years did I realize that most people are not in pain all the time. I would crash down from exhaustion at night, and in the morning I’d wake up with insane knee pain. However, everyone dismissed saying: ‘it’s psychosomatic’ or ‘get over it and go to school’ so I went along”. Too often women have encountered a situation where they were diagnosed with fibromyalgia by a rheumatologist, after a health professional, such as a family doctor, questioned their disease: “Mostly it’s regarded as something psychosomatic that is affected by emotions. My family doctor laughed at my face, telling me: ‘you’re looking for all kinds of invented diseases, so here’”. Despite empirical evidence indicating the burden of pain as a disease, there is a lack of definitive recognition of the pathological nature of this condition. Our study data show a lack of trust in fibromyalgia patients as they have no visible symptoms. They feel that they are not seen and most people do not understand their difficulties. They are denied medical and legal rights and their human dignity is harmed. Thus, a clear definition of pain as a disease and recognition of fibromyalgia specifically as a disease, are essential to raise awareness of a global health problem. Fibromyalgia does not receive the attention it deserves due to perception that fibromyalgia belongs to the realm of symptoms existing only in the patient’s brain. Thus, no interventions are made regarding the acceptance of the existence of the disease, which creates dissonance towards the patients.

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Quality of life of patients with rheumatoid arthritis and comorbid fibromyalgiaNazhabat Melikova^{1,2}, Elena Filatova², Ekaterina Filatova¹, Alexander Lila¹
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Objective. To evaluate the impact of comorbid fibromyalgia (FM) on the quality of life (QoL) of patients with rheumatoid arthritis (RA).

Methods. 90 patients with RA were included in the study. FM was diagnosed according to the ACR 2016 criteria. The presence and severity of follow symptoms were estimated: fatigue (by FSS), anxiety and depression (HADS), sleep disturbances (PSQI), cognitive impairments (DSST), symptoms of central sensitization (CSI) and the neuropathic component of pain (PD, DN4). The pain intensity was assessed by 10 cm VAS at rest. The QoL was assessed using the EQ-5D questionnaire.

Results. FM was detected in 46 RA patients (51.1%), who made up the FM(+) group. The average pain intensity was 7 and 4 cm ($p=0.001$) in the FM(+) and FM(-) groups respectively. The average scores of the CSI (50 vs. 38.5 ($p=0.001$)) and the PD questionnaire (17 vs. 11 points ($p=0.001$)) were higher in the FM(+) group. Significant differences in groups were revealed in terms of fatigue ($p=0.003$), anxiety ($p=0.001$), sleep quality ($p=0.001$) and cognitive impairments ($p=0.021$). The QoL of patients with FM was lower (0.52 vs. 0.59, $p=0.003$). Correlation between the EQ-5D-index and parameters – VAS, FSS and PD was significant in both groups. We also detected significant correlation between EQ-5D-index and CSI, DN4, HADS-T in the FM(+) group.

Conclusions. Comorbid FM significantly reduces the QoL of RA patients. The main factors affecting QoL in patients with RA and FM were the intensity and neuropathic phenotype of pain, the fatigue and anxiety.

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Effects of the COVID-19 pandemic on individuals with fibromyalgia – a systematic scoping review protocolTali Sahar, MD, MSc¹, Ali Jalali, MD^{1,3}, Sylvie Toupin, RN, BSc¹, Maria Verner, MSc¹, Sabrina Mitrovic, BSc¹, Amir Minerbi, MD, PhD², Yoram Shir, MD¹, Mary-Ann Fitzcharles, MB ChB¹, M. Gabrielle Pagé, PhD^{1,4,5}
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Background. The COVID-19 pandemic has affected people worldwide in multiple ways. Some suffered infection of varying severity and many experienced stressors associated with quarantine restrictions, lockdowns, and the consequences of social distancing. An initial literature search indicates that the pandemic had different and sometime contradicting effects on individuals with fibromyalgia; while some people experienced worsening of symptoms, others reported symptom relief because of the reduced pace and demands of daily life.

Objective. The objectives of this review were to systematically search databases and identify studies that examined the effects of COVID-19 pandemic on symptomatology of adults who had fibromyalgia prior to the pandemic, in order to map the existing knowledge and identify knowledge gaps.

Inclusion criteria. Any studies that explored the experience of adults with fibromyalgia syndrome during the COVID-19 pandemic. We will review only studies with participants who were diagnosed with fibromyalgia prior to the pandemic.

Methods. This scoping review followed the recommendations of Preferred Reporting Items for Systematic Review and Meta-Analyses for Scoping Review (PRISMA-ScR). We used pilot search, to develop a full search strategy for Medline, Embase, CINAHL and PsycInfo (searched until July 2022). The reference list of all included sources of evidence were screened for additional studies. Sources of unpublished studies were searched: clinical trial.gov, OPENGREY.EU and MedRxiv. Studies in any language were included. Abstracts and full-text articles were screened for inclusion by two reviewers. Similarly, two independent reviewers systematically extract the data from the included articles. Disagreements in any stage were resolved through consensus.

Results. Twenty studies out of 246 articles met the inclusion criteria. They included 4631 participants with Fibromyalgia (The number of participants ranged between 17 to 1156 in each study), the mean age was 46.01 (range 17-60). Most studies were conducted at the acute phase or sub-acute phase of the pandemic (16 studies), and majority took place in Europe (13 studies). Only five studies have studied the same cohort before and after the pandemic. Interestingly, these studies had mixed results; while the pandemic had negative impact on most or some of the participants, some reported positive outcomes.

Conclusion. The effects of the COVID-19 pandemic on individuals with fibromyalgia were studied mainly in Europe and during the acute phase of the pandemic; While majority of surveys reported negative effect on individuals with fibromyalgia, longitudinal studies had mixed results; Further research is needed to explore the long-term effects and the factors that have contributed to positive effects for some individuals with fibromyalgia.

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