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Review Article

Physiotherapy Section

The Effect of Pain Neuroscience Education in the Treatment of Fibromyalgia: A Narrative Review

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ABSTRACT

Pain Neuroscience Education (PNE) is a widely used approach for educating patients with chronic musculoskeletal conditions. It has shown significant improvements in pain levels, disability and psychosocial outcomes, particularly when combined with exercise and manual therapy. Several studies have emphasised the effectiveness of PNE in reducing pain and enhancing the quality of life in individuals with Fibromyalgia (FM). This literature review aimed to systematically assess the effectiveness of PNE in individuals with FM. A comprehensive literature search was conducted using electronic databases, including Google Scholar, PubMed, ResearchGate and ScienceDirect, to identify studies examining the impact of PNE on FM. The review concluded that PNE alone did not significantly benefit patients with FM. However, when integrated with other group interventions, such as physical therapy or exercise therapy, PNE was more effective in reducing the impact of psychosocial variables and pain intensity compared to either treatment alone.

Keywords: Central sensitisation, Chronic musculoskeletal conditions, Psychosocial variables

INTRODUCTION

The FM is a prevalent aetiology of prolonged, diffuse musculoskeletal pain, which is accompanied by stiffness, sleep disturbances, fatigue and chronic pain [1]. FM is a complicated condition with no known biological cause. Research aimed at identifying reliable, high-tech biomarkers to differentiate it from other rheumatic diseases has not yet yielded an objective test with sufficiently high sensitivity and specificity for therapeutic purposes. The pathophysiology and causes of FM remain unclear. However, a growing body of research has recognised FM as a disease related to pain with a neurobiological foundation [2]. Fibromyalgia Syndrome (FMS) was first described in the 19th century, initially referred to as "fibrositis" by Gowers. It was later classified as a "pain syndrome" by Graham in 1950. Diagnostic standards were developed in 1990 [3].

The exact cause and underlying mechanisms of FM remain unclear. Nonetheless, an increasing body of research supports its identification as a clinically diagnosed pain disorder rooted in neurobiology. Individuals with FM often suffer from widespread hyperalgesia, which refers to heightened pain sensitivity to painful stimuli and allodynia, defined as pain triggered by normally non painful stimuli, alongside chronic pain. These indications suggest a sensory processing issue. Furthermore, brain atrophy has been connected to FM [2]. Despite the absence of a cure for FM, individuals can regain control and experience significant improvements with the right knowledge, lifestyle adjustments and medication. Approaches to managing adult pain, such as cognitive, behavioural and operant methods, are based on models that consider behavioural, emotional, cognitive and biological factors. Recently, more research has been conducted on pain education, with a focus on PNE. PNE is a teaching tool used by physical therapists to educate patients about the physiological and biological mechanisms underlying their pain [4]. This narrative review aims to systematically examine the existing evidence on the efficacy of PNE in treating FM. By analysing and synthesising findings from recent clinical trials, observational studies and patient testimonials, we seek to provide a comprehensive overview of the potential benefits and limitations of PNE. Through this review, authors aim to elucidate the role of PNE in the multidisciplinary treatment framework for FM, offering insights into its impact on pain perception, patient empowerment and overall quality of life.

Pathophysiology

The FM is a neurosensory disorder in which the person's brain is unable to process pain [5]. The pathophysiology of FM involves abnormal pain signalling, genetic predispositions, neuroendocrine and autonomic dysfunction, environmental triggers and sleep disturbances. Its pathogenesis is unclear, with diagnosis based on clinical evaluation. Enhanced pain sensitivity and widespread pain likely result from altered central sensory processing and impaired endogenous pain inhibition [3].

Abnormal pain processing in FM [3]: FM is a complex chronic pain condition with an unclear pathophysiology, characterised by abnormal central nervous system processing, impaired pain modulation and molecular changes in pain pathways. Patients experience heightened sensitivity to various stimuli (pressure, heat, and cold) due to central augmentation of sensory input rather than traditional Central Sensitisation (CS) [3].

Central nervous system alterations: Structural and functional changes: A 2014 review by Cagnie B et al., identified grey matter reductions in the Anterior Cingulate Cortex (ACC) and prefrontal cortices, increased cortical blood flow to pain-processing areas, and reduced connectivity in the descending pain-modulation system involving the ACC, amygdala, hippocampus and brainstem [6].

Descending pain pathway disruption: This pathway, comprising the ACC, Periaqueductal Grey (PAG), and Rostral Ventromedial Medulla (RVM), modulates pain via endogenous opioid release and serotonergic and noradrenergic activity. Chronic pain disrupts this system, reducing opioid release and altering serotonin and noradrenaline secretion [7].

Molecular and Neurotransmitter Dysregulation

Pain signal transmission: Pain signals are mediated by A-delta and C-fibres, which release glutamate and substance P in the dorsal horn, activating the ascending spinothalamic tract. Opioids inhibit these signals by binding to Mu-Opioid Receptors (MOR), decreasing the release of glutamate and substance P and enhancing descending inhibitory pathways.

Chronic pain adaptations: Persistent C-fibre stimulation leads to apoptosis of inhibitory interneurons, increased excitatory

neurotransmitters (glutamate and substance P), and reduced endogenous opioid and serotonin levels. This "wind-up" phenomenon underlies central pain sensitisation, allodynia and hyperalgesia [8].

Secondary Mechanisms

- **Neurotransmitter and hormonal imbalances:** FM patients exhibit reduced serotonin levels, which contribute to mood disturbances and altered pain modulation. GABAergic dysfunction in the PAG may further impair serotonin regulation [9].
- **Autonomic Nervous System (ANS) abnormalities:** Dysregulation in the ANS manifests as impaired microcirculatory responses and vasoconstriction, exacerbating stress sensitivity, elevated pain perception and diminished Growth Hormone (GH) and Insulin-Like Growth Factor-1 (IGF-1) production [10].

Clinical Features of FM [2]:

- **Musculoskeletal system:**
  Chronic pain
  Morning joint stiffness
  Fatigue
  Intolerance to exercise
- **Autonomic nervous system:**
  Allodynia
  Paraesthesia
- **Psychiatric symptoms:**
  Mood swings
  Depression
  Anxiety
- **Sleep disorders:**
  Insomnia
  Frequent awakenings
- **Cognitive system:**
  Memory deficits
  Difficulty in concentrating
- **Digestive system:**
  Dyspepsia
  Irritable bowel syndrome

Diagnostic Criteria [11]

2016 American College of Rheumatology Fibromyalgia Diagnostic Criteria:

1. Generalised pain, defined as pain in at least four of five regions, is present.
2. Symptoms have been present at a similar level for at least three months.
3. The widespread pain index score is ≥7, the symptom severity scale score is ≥5, the widespread pain index score is 4 to 6, and the symptom severity score is ≥9.

A diagnosis of FM is valid irrespective of other diagnoses. A diagnosis of FM does not exclude the presence of other clinically important illnesses.

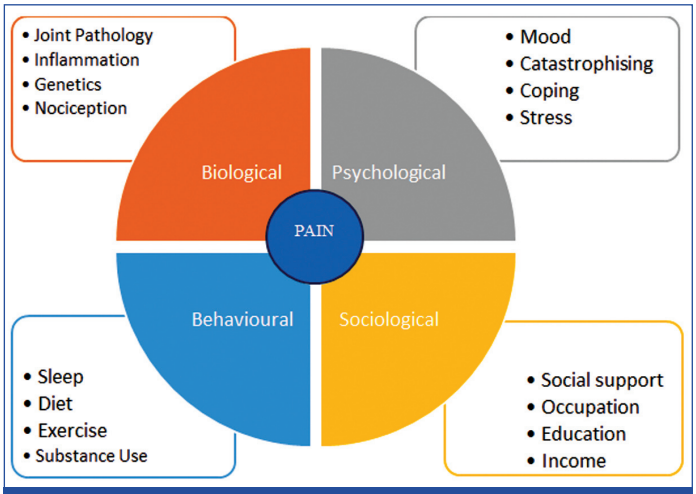
Treatment Approaches for FM

The FM currently has no definitive cure and treatment is primarily aimed at managing symptoms and enhancing quality of life. This strategy involves a comprehensive multidisciplinary approach, including pharmacological interventions, lifestyle changes and other complementary therapies. While pharmacological treatment is commonly recommended, it often comes with side-effects and receives a low level of endorsement. In the last few years, interest has increased in non drug therapies, especially physical therapy, as alternative treatments that present little to no side-effects for patients.

Pain Neuroscience Education (PNE): As an educational intervention, PNE is often combined with different physical and movement-based therapies, such as exercise. Current evidence indicates that integrating PNE with movement or exercise is more effective than using educational methods alone for reducing pain and disability [12].

In recent years, pain education has gained attention among researchers and healthcare professionals. This type of instruction is referred to as PNE. PNE serves as a teaching resource for physiotherapists, helping patients understand the physiological and biological processes that contribute to their pain [12].

[Table/Fig-1] illustrates biological, psychological, sociological and behavioural factors associated with pain. This model of pain also provides the best foundation for tailoring the most comprehensive pain management programme for each specific patient [13].



[Table/Fig-1]: Biopsychosocial model of pain.

Biological Factors Behind Pain [14]

The complex process of pain is impacted by social, psychological and biological variables. It falls into four categories: immunological, neurological, endocrine and genetic.

Genetics significantly contributes to chronic pain through complex interactions involving serotonergic, glutamatergic, GABAergic, cytokine and growth factor genes. Epigenetic changes related to pain can be influenced by factors such as physical activity and psychological stress, as suggested by the field of epigenetics. Gene expression is affected by both genetic factors and environmental influences. Physicians can educate patients about the possibility of genetic predisposition to hypersensitivity while emphasising the importance of ecological and daily routine factors in determining pain sensitivity.

Neural factors, such as gate theory, underscore the significance of alterations in neural processing in how pain is perceived. The biology of pain affects the brain and spinal cord, influencing pain perception. Stress can lead to conditions like allodynia, hyper- or hypoalgesia, and heightened nerve sensitivity, contributing to stress intolerance. Understanding the relationship between sleep disturbances and chronic pain is crucial for delivering comprehensive education on pain neuroscience. Chronic pain is also influenced by immune factors, such as immune mediators and inflammatory molecules. For optimum results, a multimodal strategy that incorporates PNE is advised.

Physiological Factors Behind FM Pain [15]

The FM involves a complex interplay of dysregulated systems contributing to chronic pain and associated symptoms:

Hypothalamic-Pituitary-Adrenal (HPA) axis dysfunction: Hypoactivity of the HPA axis in FM disrupts cortisol regulation,

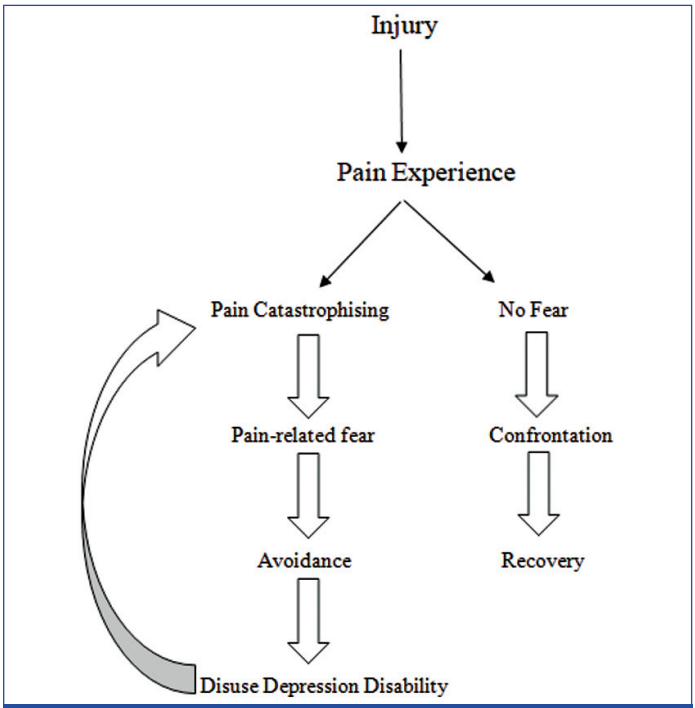
leading to fatigue, reduced motivation and post-exercise malaise. Exercise may help restore HPA axis balance.

Glial cell activation: Heightened glial activation in the brain and spinal cord increases sensory hyperexcitability by reducing glutamate regulation, overstimulating N-methyl-D-aspartate (NMDA) receptors and elevating Tumour Necrosis Factor alpha (TNF-α) levels, which correlates with pain, depression and anxiety.

Cytokine dysregulation: Central Sensitisation (CS), driven by cytokine-related amplified neuronal signalling and NMDA receptor activation, underpins FM symptoms such as pain, fatigue and cognitive dysfunction.

Neurotransmitter imbalances: Serotonin and noradrenaline deficiencies impair pain modulation, sleep and mood, while elevated glutamate enhances pain signalling via NMDA and AMPA receptor activation. In FM, serotonin deficiency contributes to hyperalgesia, sleep disturbances, and increased substance P levels. Dysfunction in serotonin and noradrenaline affects pain perception, sleep, mood and cognition, exacerbating FM's motor, psychological and pain symptoms.

The [Table/Fig-2] illustrates two contrasting pathways in response to pain experience: a maladaptive cycle of fear avoidance and a positive recovery trajectory [16]. As mentioned above, [Table/Fig-2] illustrates two contrasting pathways in response to pain experience: a maladaptive cycle of fear avoidance and a positive recovery trajectory.



[Table/Fig-2]: The process of pain recovery.

Following an injury, individuals may either develop a fear-avoidance response or a confrontational approach. In the fear-avoidance cycle, the pain experience is magnified by pain catastrophising, driven by negative emotions and threatening illness-related information. This leads to pain-related fear, avoidance behaviours and ultimately disuse, depression and disability, perpetuating the cycle of pain and dysfunction. In contrast, if the individual confronts the pain without fear, this approach can lead to recovery by breaking the cycle of avoidance and promoting functional improvement. The figure highlights the critical role of cognitive and emotional factors in shaping pain outcomes and the importance of addressing these aspects in treatment.

Delivery Methods of PNE [17]

PNE is an educational approach led by physical therapists that aims to inform individuals experiencing pain about the biological and physiological factors that play a role in their discomfort.

1. Reading educational materials: Books, articles, or online resources that explain pain mechanisms can help patients better understand the biological and physiological processes involved in their discomfort.

2. Online videos and apps: Educational videos or apps that illustrate pain science concepts through animations, diagrams and simplified explanations can help patients visualise how their pain is generated and processed.

3. Use of metaphors and analogies: Patients can use metaphors and analogies that resonate with them personally, like thinking of pain signals as a car alarm that goes off too easily, to reframe their understanding of pain in a more manageable way.

4. Journaling or reflection: Writing about pain experiences and tracking patterns can help patients connect their pain to specific triggers and better understand how emotions, thoughts, or activities affect their pain.

5. Social support groups: Engaging in online or in-person support groups where people share similar experiences can reinforce educational messages, provide reassurance and help normalise their pain experience.

By engaging with these resources, patients can continue to educate themselves on pain science, empowering them to manage their condition more effectively.

Dosage of PNE: According to a study on dosage guidelines for pain education in FM conducted by Amer-Cuenca JJ et al., (2019), both PNE and biomedical education significantly reduce FM patients' mechanical hyperalgesia (such as elevated PPTs), pain catastrophising and pain anxiety. However, neither intervention had any effect on temporal summation. Additionally, in this population, biomedical education and higher doses of PNE (six 45-minute sessions) had a greater effect on pain intensity than lower doses (two 45-minute sessions or six 15-minute sessions) [18].

Methodology

This narrative review was designed to systematically assess the effectiveness of PNE in individuals with FM. A search was conducted using electronic databases, including Google Scholar, PubMed, ScienceDirect and ResearchGate. The keywords used in the search were "FM," "pathophysiology," "pain," "CS," "PNE," and "signs and symptoms of FM." The literature search yielded seven unique and relevant studies that were included in the review.

Inclusion criteria: Patients diagnosed with FM, articles published between 2014 and 2024, inclusion of both male and female participants, and a focus on pain.

Exclusion criteria: Articles were excluded if they were published in languages other than English, did not include PNE, or if the full text was unavailable.

RESULTS

[Table/Fig-3] summarises the studies included in the narrative review [19-25].

DISCUSSION

This study sought to gather recent literature on the application of PNE for treating individuals with FM and chronic musculoskeletal pain, aiming to enhance understanding of this approach. A total of seven relevant articles were identified for this investigation.

Of the articles reviewed in this study, the majority showed results indicating that PNE, when added to a multimodal treatment, demonstrated positive results in reducing pain, catastrophisation, and kinesiophobia. However, PNE on its own did not demonstrate any significant improvements in reducing pain intensity or psychosocial factors.

S. No.	Author, year	Title	Method	Results	Conclusion
1	Kircali S et al., 2024 [19]	Pain Neuroscience Education (PNE) and motor imagery-based exercise protocol for patients with FM	A randomised controlled trial	The study found a statistically significant decrease in pain intensity across all experimental groups, with no group showing superior results (VAS: Motor Imagery-based Exercise Protocol (MIEP) + Pain Neuroscience Education (PNE), p-value=0.003; MIEP, p-value=0.003; PNE, p-value=0.002). Additionally, significant improvements in organic pain beliefs were observed in the groups receiving PNE (MIEP + PNE, p-value=0.017; PNE, p-value=0.003). The MIEP + PNE group demonstrated significant superiority in reducing organic pain beliefs compared to the control group (p-value=0.008)	The study found that MIEP and PNE, individually and combined, reduced pain intensity. MIEP improved motor imagery, body awareness and pain levels, while PNE enhanced pain beliefs, reduced fear and negative thoughts and improved psychological and emotional regulation.
2	Cuenca-Martínez F et al., 2023 [20]	Pain Neuroscience Education (PNE) in patients with chronic musculoskeletal pain	Umbrella review	Adding a PNE-based intervention to other treatments, such as exercise, results in better clinical outcomes than using a multimodal approach alone. This findings indicate a reduction in the impact of psychosocial variables	Adding PNE to other treatments improves clinical outcomes compared to physical therapy or exercise alone, particularly in reducing the impact of psychosocial variables. However, PNE alone did not significantly improve pain intensity, disability.
3	Areso-Boveda PB et al., 2022 [21]	Effectiveness of group intervention using Pain Neuroscience Education (PNE) and exercise in women with Fibromyalgia (FM)	Pragmatic non randomised controlled trial.	The study shows that a group intervention based on PNE, preceded by an active-listening interview and accompanied by exercises of increasing intensity, can improve, among other factors, the severity of symptoms, the functional capacity and the impact of pain in the daily life of women with FM. This improvement was sustained for 1 year	The findings indicate that this intervention based on PNE and exercise is feasible and effective in patients with Fibromyalgia (FM) in real-world practice in PC, and may be the ideal level of care for this patient population
4	Barrenengoa-Cuadra MJ et al., 2021 [22]	Effectiveness of a structured group intervention based on pain neuroscience education for patients with Fibromyalgia (FM) in primary care	A multicentre randomised, open- label, controlled trial.	A randomised controlled trial found that a structured group intervention based on PNE effectively reduced the impact of FM on pain, anxiety and catastrophising thoughts compared to treatment as usual alone	The addition of a PNE intervention resulted in significant improvements in quality of life and symptom control in this patient sample, matching or exceeding previously reported outcomes.
5	Serrat M et al., 2020 [23]	Effectiveness of a multicomponent treatment for FM Based on Pain Neuroscience Education (PNE), Exercise therapy, psychological support, and nature Exposure (NAT-FM)	A pragmatic randomised control study	Data analysis showed that TAU + NAT-FM was a more effective adjuvant therapy for FM patients than TAU alone. TAU + NAT-FM had a significant post-treatment effect on functional impairment, pain, fatigue, anxiety, depression and physical function, as well as process variables like kinesiophobia, pain catastrophising thoughts, personal perceived competence and cognitive emotion regulation subscales	This study suggests that the TAU + NAT-FM intervention (added to TAU) could be a promising add-on therapy for this costly disease. It not only improves symptoms but also benefits society and the economy by reducing the use of public resources and job losses.
6	Pires D and D Costa, 2014 [24]	A Pain Neuroscience Education (PNE) program for FM patients with cognitive defects	Case study	The study found a significant decrease in pain (7.22±1.3 to 4.22±1.7, p-value=0.018), kinesiophobia (36.5±8.7-24.4±4.2, p-value=0.011), catastrophisation (35.6±10.6 to 16.1±9.5, p-value=0.008)	This case study suggests that a Pain Neuroscience Education (PNE) program can reduce pain and maladaptive pain cognition in FM patients.
7	van Ittersum MW, 2014 [25]	Written Pain Neuroscience Education (PNE) in FM	A multicentre randomised controlled trial	In the PNE group, there was a significant increase in FM-related symptoms (p-value=0.02) and perceived stiffness (p-value=0.03) in the three weeks before the intervention. In the RE group, patient's belief in treatment effectiveness (p-value=0.03), attribution of FM symptoms to chance (p-value=0.02) and pain severity decreased (p-value=0.02)	Based on study limitations and literature, it is concluded that written Pain Neuroscience Education (PNE) is ineffective in reducing the impact of FM on daily life, pain catastrophising and illness perceptions in patients. Patients with FM require one-on-one sessions to understand pain neuroscience.

[Table/Fig-3]: Summary of the relevant studies [19-25].

A 2013 double-blind randomised controlled trial by Van Oosterwijck J et al., found that education on pain physiology can have positive effects on pain, disability and catastrophisation in patients with FM. The results suggest that FM patients can understand and retain complex information about pain physiology. Pain physiology education is an effective treatment component, improving health outcomes and enhancing long-term endogenous pain inhibition [26].

A promising approach for managing chronic pain like FM is PNE. This method aims to enhance patients' ability to cope with pain, reduce fear-avoidance behaviours and improve their overall wellbeing by providing insights into the scientific understanding of pain. Despite its increasing popularity, further research is needed to fully understand its effectiveness and optimise its use.

CONCLUSION(S)

This narrative review suggests that PNE alone does not offer any therapeutic advantages for patients with FM. However, when combined with other group interventions like physical therapy or exercise therapy, PNE has been effective in reducing the impact of psychosocial factors and pain intensity in individuals suffering from FM and chronic musculoskeletal pain. This combined approach is more beneficial than using these treatments in isolation.

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