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Neuroscience-based approaches in chronic pain management: integration of mind-body interventions in rehabilitation

Hyunjoong Kim*

Department of Senior Exercise Prescription, Gwangju Health University, Gwangju 62287, Republic of Korea

***Correspondence:** Hyunjoong Kim, Department of Senior Exercise Prescription, Gwangju Health University, Bungmun-daero 419beon-gil, Gwangju 62287, Republic of Korea. hjkim@ghu.ac.kr

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Abstract

Chronic pain, affecting approximately 30.3% of adults worldwide, presents a significant global health issue, severely impacting individuals' quality of life and creating substantial socioeconomic challenges. Traditional pain management methods, such as physical therapy and pharmacological treatments, primarily focus on the biological aspects of pain while often neglecting the psychological and social factors. However, recent advancements in neuroscience have revealed that chronic pain is influenced by changes in the central nervous system, including mechanisms like central sensitization and neuroplasticity. This paper examines contemporary neuroscience-informed interventions, including Pain Neuroscience Education (PNE), mindfulness practices, and cognitive functional therapy (CFT), which target these neurobiological changes to improve pain perception and behaviors. These interventions help rewire the brain's pain pathways, promoting long-term pain relief and functional recovery. Additionally, combining neuroscience-based approaches with conventional therapies has been shown to enhance treatment outcomes. This work emphasizes the need for personalized approaches and the integration of emerging technologies to enhance the accessibility and effectiveness of chronic pain management.

Keywords

Neuroplasticity, neuroscience, pain management, rehabilitation

Introduction

Chronic pain, defined as pain persisting for over three months, is a significant global health concern that impacts approximately 30.3% of adults worldwide [1]. Musculoskeletal chronic pain, in particular, not only diminishes individuals' quality of life but also leads to substantial socioeconomic challenges, including increased healthcare expenditures and reduced workforce productivity [2]. The World Health Organization estimates that chronic pain results in an annual global economic loss of approximately $500 billion [3].

Traditional approaches in rehabilitation medicine for managing chronic pain have focused on strategies like physical therapy, exercise therapy, and pharmacological treatments [4]. While these methods primarily target the biological aspects of pain, they often overlook the psychological and social dimensions that contribute to the overall pain experience [5]. Recent advancements in neuroscience have demonstrated that chronic pain is a multifaceted condition, strongly linked to alterations in the central nervous system (CNS) [6, 7].

In light of these findings, neuroscience-informed interventions have gained increasing attention within the rehabilitation field [8]. Techniques such as Pain Neuroscience Education (PNE), mindfulness practices, and cognitive functional therapy (CFT) have shown effectiveness in reshaping pain perception and encouraging adaptive behaviors among individuals with chronic pain [9, 10]. These interventions utilize the principle of neuroplasticity to rewire pain-related neural pathways and manage central sensitization effectively [10–12].

This paper aims to explore the neuroscientific foundations and clinical applications of contemporary interventions in chronic pain management. It provides a systematic review of the neurobiological mechanisms, practical implementation protocols, and long-term efficacy of these methods, offering clinicians valuable insights for integrating these approaches into practice.

Neurobiological basis of chronic pain

Understanding the neurobiological mechanisms of chronic pain forms the cornerstone for developing modern intervention strategies [13]. Recent advancements in neuroscience have revealed that chronic pain extends beyond peripheral tissue damage or inflammatory responses, involving complex changes within the CNS [14].

The concept of the pain neuromatrix explains that pain is not merely a sensory experience but the result of the activation of a multidimensional neural network [15]. This network includes interactions among various brain regions such as the somatosensory cortex, anterior cingulate cortex, and insula, integrating the sensory, emotional, and cognitive dimensions of pain [16].

Central sensitization, one of the key mechanisms of chronic pain, refers to increased CNS sensitivity in processing pain signals [7]. This phenomenon involves changes in synaptic plasticity, heightened activation of NMDA receptors, and impaired descending pain modulation systems [17]. Consequently, the pain threshold is lowered, leading to phenomena such as hyperalgesia (heightened pain sensitivity) and allodynia (pain from normally non-painful stimuli) [18].

Neuroplasticity is a critical concept for understanding the structural and functional changes in the brain associated with chronic pain [19]. Functional magnetic resonance imaging (fMRI) studies have documented cortical thickness alterations, decreased gray matter density, and rewiring of neural circuits in chronic pain patients [20]. Importantly, these changes are often reversible, highlighting the potential for recovery through therapeutic interventions [21].

Psychosocial factors influencing pain experiences also have distinct neurobiological underpinnings [22]. Emotional states such as stress, anxiety, and depression enhance pain sensitivity through activation of the hypothalamic-pituitary-adrenal (HPA) axis and may also impact immune system function [23]. Additionally, social support and environmental factors are known to modulate endogenous pain control systems [24–26].

The recognition of these psychosocial influences has led to the development of targeted interventions that specifically address these factors while acknowledging their neurobiological underpinnings. The following section explores how contemporary mind-body interventions effectively integrate this understanding into practical therapeutic approaches.

Contemporary mind-body and neuroscience-based interventions

Contemporary chronic pain management involves the development and application of various interventions based on the complex neurobiological mechanisms of pain. These interventions target neuroplasticity and CNS changes, aiming for long-term pain control and functional recovery [27]. Central sensitization, commonly observed in chronic pain patients, encompasses neuroplastic changes in the spinal dorsal horn and higher CNS structures, leading to a lowered pain threshold, amplified pain signals, and expanded pain perception areas [7, 17].

PNE

PNE is an educational intervention designed to explain the biological and physiological processes of pain in an accessible manner for patients [9]. Its primary goal is to reduce misconceptions and fear associated with pain while enhancing patients' self-efficacy in managing their condition. Neuroimaging studies indicate that PNE alters activation patterns in the prefrontal cortex and limbic system, leading to the reorganization of pain perception and processing pathways [8, 28].

Key educational topics in PNE include the biopsychosocial model of pain, the concept of central sensitization, the relationship between pain and tissue damage, and the neuroplasticity of the nervous system [29]. Recent studies have demonstrated PNE's effectiveness across various chronic pain conditions, such as chronic low back pain, fibromyalgia, and chronic widespread pain [9–12, 30]. The educational process employs tools like visual metaphors, real-life examples, and interactive explanations to enhance patient comprehension and engagement [31].

Neurological changes and therapeutic implications

Understanding the structural and functional brain changes in chronic pain patients forms the basis of therapeutic approaches. Changes in executive function within the prefrontal cortex influence decision-making and behavior regulation [32], while hyperactivation of the amygdala heightens anxiety and fear responses related to pain [33]. Alterations in self-referential processing in the posterior cingulate cortex affect the personal meaning and interpretation of pain, and changes in the insula modulate interoception and pain perception [34, 35].

These neurological changes are reversible, and appropriate interventions can reconfigure them positively [5]. Structural and functional connectivity changes in the brain are considered critical mechanisms in pain chronification, offering new therapeutic targets [18].

CFT

CFT is an integrated approach that addresses pain-related neurological changes through cognitive restructuring, behavior modification, and movement retraining [36]. CFT aims to identify and correct maladaptive beliefs, fear-avoidance behaviors, and dysfunctional movement patterns in patients [37].

The therapy comprises three main stages: first, understanding and evaluating individual factors related to the patient's pain experience; second, modifying maladaptive behaviors and beliefs; and third, relearning functional activities and movements [38]. During the movement retraining phase, improvements in motor cortex reorganization and functional connectivity in sensory processing regions are observed [39, 40].

Complementary approaches

Mindfulness-based interventions emphasize nonjudgmental attention to present experiences, effectively modulating emotional and cognitive responses to pain [41]. fMRI studies show that mindfulness practice regulates activation in the anterior cingulate cortex and insula while enhancing top-down pain modulation networks [42].

Meditation and breathing techniques play a crucial role in balancing the autonomic nervous system and managing stress responses [43]. Practices such as slow breathing and mindfulness meditation regulate HPA axis activity, reducing pain sensitivity [44], leading to decreased cortisol levels and improved immune function [45]. These techniques are also effective in alleviating pain-related anxiety and depressive symptoms [46]. However, several limitations should be considered. Implementation challenges include variable patient engagement, resource constraints, and the need for specialized training. Additionally, the effectiveness of mindfulness interventions may vary significantly among different patient populations, and long-term adherence remains a concern.

Virtual reality and augmented reality interventions

Virtual reality and augmented reality technologies provide innovative approaches to pain management [47]. Beyond simple distraction, these technologies function as therapeutic tools by modifying somatosensory representations in the brain and facilitating motor relearning [48]. Neuroimaging studies reveal that VR interventions regulate activity in pain-related brain regions, particularly the anterior cingulate cortex, and insula while activating endogenous analgesic systems [49].

VR is especially effective in creating a safe environment that reduces fear of movement and encourages gradual engagement in physical activities for chronic pain patients [50]. AR, on the other hand, integrates therapeutic elements into real-world environments, enabling patients to adopt pain management strategies more effectively in daily life [51].

Motor imagery and graded motor imagery

Motor imagery and graded motor imagery (GMI) are effective interventions that promote motor cortex reorganization without actual movement [52]. GMI consists of three progressive stages: laterality recognition, explicit motor imagery, and mirror therapy. Each stage incrementally activates neural networks involved in motor planning and execution [53]. These approaches have shown particular efficacy in managing chronic pain conditions such as complex regional pain syndrome [54].

Biofeedback and neurofeedback

Biofeedback and neurofeedback enable real-time monitoring and regulation of physiological states [55]. These techniques empower patients to self-regulate autonomic nervous system functions. For instance, electromyography biofeedback is effective in controlling muscle tension and reducing pain [56]. Neurofeedback directly targets pain processing networks by allowing patients to voluntarily modulate brainwave patterns, offering a novel avenue for intervention [57].

Body awareness techniques

Body awareness techniques approach pain management by enhancing proprioception and interoception [58]. Methods such as the Alexander Technique and Feldenkrais Method emphasize strengthening the mind-body connection and correcting inefficient movement patterns [39]. These techniques have been shown to promote reorganization of the somatosensory cortex and normalization of body schema [8], improving body awareness and self-regulation in chronic pain patients [5].

Clinical integration and implementation

Effective chronic pain management necessitates the systematic clinical application of neuroscience-based interventions. Notably, the integration of multiple interventions has demonstrated superior therapeutic outcomes compared to single-modality approaches [59] (Figure 1).

Multimodal approach

Neuroscience-based interventions are more effective when combined with other therapeutic modalities. For instance, the combination of PNE with exercise therapy yields better results in pain reduction and functional improvement compared to each intervention alone [60]. Similarly, incorporating mindfulness or CFT into traditional physical therapy has been shown to enhance the reorganization of pain-related neural networks [61]. This multimodal approach addresses the multidimensional nature of chronic pain and promotes changes at various levels of the CNS [31]. Furthermore, recent studies suggest that integrating emerging technologies, such as virtual reality or biofeedback, with conventional treatments can enhance patient engagement and therapeutic outcomes [62].

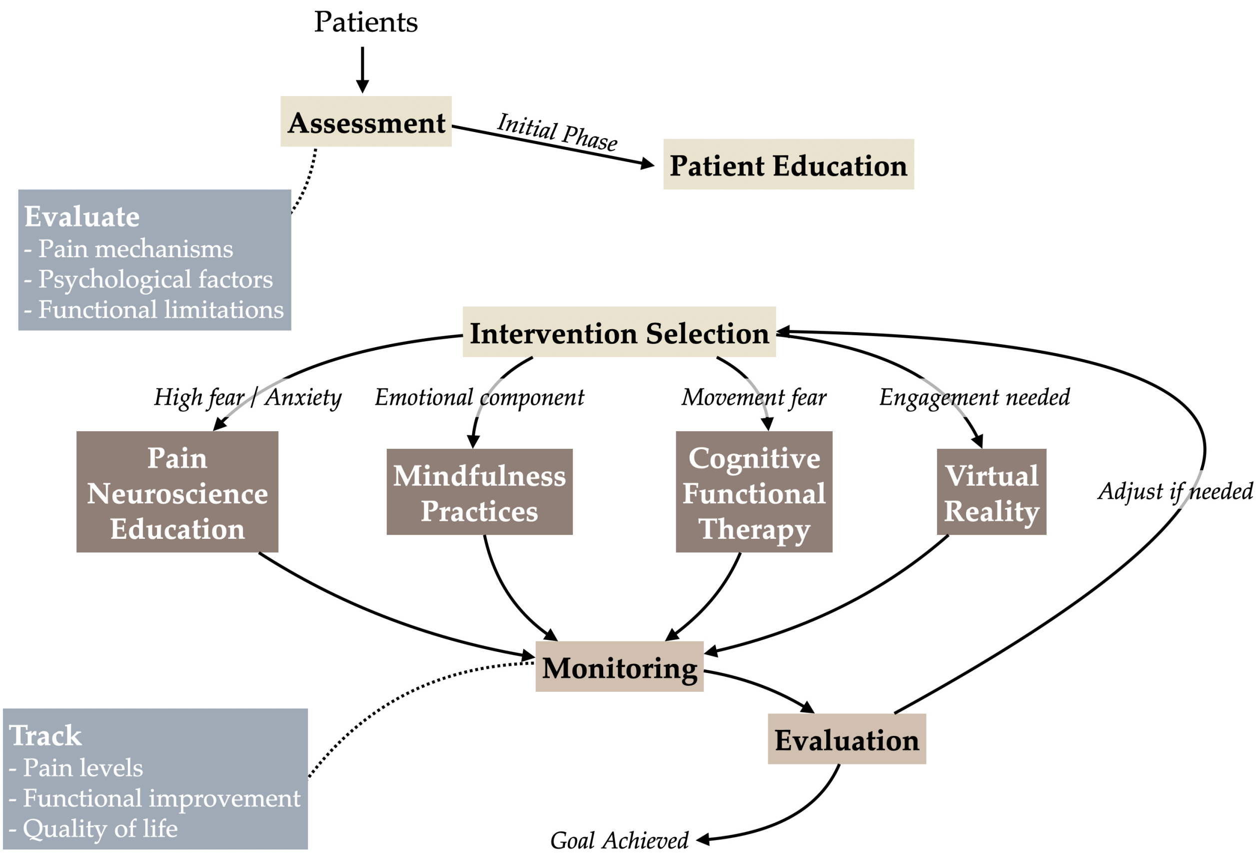

Figure 1. Clinical implementation flowchart

Patient selection and clinical decision-making

To optimize the effectiveness of interventions, tailored approaches that consider individual patient characteristics and conditions are crucial. Assessing factors such as the degree of central sensitization, psychosocial influences, and cognitive receptiveness is essential in determining the appropriate combination of interventions [63]. Research shows that personalized approaches improve treatment efficacy and patient satisfaction [64]. Clinical decision-making should encompass not only the patient's pain mechanisms but also functional demands in daily life, personal goals, and social support systems [4].

Implementation strategies and treatment algorithms

In clinical practice, systematic treatment algorithms are used to determine the sequence and intensity of interventions. Initial evaluations should comprehensively assess the neurobiological characteristics of pain, as well as the patient's beliefs, expectations, and living environment [65]. Based on this, stepwise and progressive intervention plans are developed and continuously adjusted according to patient responses [66]. Regular re-evaluations and feedback during the treatment process are essential for monitoring intervention efficacy and refining therapeutic strategies as needed [67]. A clinical case study by Caneiro et al. [68] demonstrated the effectiveness of integrated neuroscience-based interventions in a 49-year-old patient with persistent low back pain. Similar to this case report, Fersum et al. [36] documented significant improvements in patients receiving CFT, with a mean pain reduction of 35–40%. The integration of PNE and mindfulness practices has also shown synergistic effects, as reported by Louw et al. [9] and Cherkin et al. [46].

Cost-effectiveness and healthcare delivery

Studies on the cost-effectiveness of neuroscience-based interventions are increasing. While these approaches may initially require more time and resources than traditional treatments, they contribute to long-term cost savings and improved quality of life [69]. Group-based programs and digital health technologies have gained attention as cost-effective delivery methods [70]. Additionally, integrating these interventions into primary care settings can enhance resource efficiency and accessibility, benefiting a broader range of patients [71].

Outcome assessment and quality measures

Evaluating the effectiveness of interventions requires comprehensive outcome measures. Beyond traditional metrics such as pain intensity, assessments should include functional performance, quality of life, changes in pain perception, and neurophysiological markers [72]. Recently, the importance of patient-reported outcome measures has been emphasized, serving as valuable tools for assessing treatment efficacy and improving the quality of care [73].

Future directions and implication

The field of neuroscience-based interventions for chronic pain is rapidly evolving, offering both new opportunities and challenges for clinical practice and research [74]. Innovations in neuroimaging are enhancing the understanding of how these interventions work at the neurobiological level, paving the way for the development of more personalized and effective treatment strategies [75].

Research priorities and emerging areas

To improve the outcomes of chronic pain management, key research areas need further exploration. One priority is a detailed understanding of the mechanisms underlying individual interventions. For example, studies should investigate how educational approaches restructure pain-related neural networks and how these changes contribute to long-term pain relief [21]. Longitudinal studies using advanced neuroimaging techniques could offer valuable insights into the dynamic effects of these interventions over time [19].

Another crucial focus is identifying the best combinations and sequences of interventions. While current evidence supports the effectiveness of multimodal approaches, additional research is required to establish detailed protocols [76]. Furthermore, studies should examine how specific intervention combinations may work differently based on individual patient profiles, such as their clinical presentation and psychosocial characteristics [63].

Clinical practice evolution and implementation challenges

The integration of neuroscience-based interventions into clinical practice requires updated guidelines that reflect recent evidence. Standardized protocols and assessment tools are essential to facilitate effective implementation [4]. Many healthcare providers also need additional training to bridge the gap between the theoretical foundations of these approaches and their practical application, highlighting the importance of comprehensive education programs [68].

However, structural challenges in healthcare systems, including limited insurance coverage, resource constraints, and time pressures, often hinder the widespread use of these interventions [77]. Moreover, transitioning from traditional biomechanical models to modern neuroscience-based approaches demands significant shifts in mindset for both clinicians and patients, requiring careful planning and support [78].

Technological integration and innovation

Emerging digital health technologies offer promising solutions to many challenges in chronic pain management. Virtual reality and augmented reality are proving to be valuable tools for enhancing pain management, particularly by supporting motor relearning and modulating pain perception [79]. Large language model-based chatbots are emerging as innovative tools for providing personalized support and guidance to patients, offering round-the-clock assistance and adaptive pain management strategies [80]. The integration of gamification elements into digital health interventions has shown the potential in improving patient engagement and treatment adherence by making therapeutic activities more engaging and rewarding [81]. Mobile health applications and wearable devices also provide opportunities for real-time monitoring, feedback, and improved patient engagement, thereby fostering better self-management and adherence to treatment [82].

Artificial intelligence and machine learning technologies are increasingly being explored for their potential to create individualized treatment plans and predict patient outcomes [83]. Advanced brain-computer interfaces offer promising opportunities for tailoring rehabilitation programs by directly measuring neural responses and adapting interventions in real time [84]. Insights gained from analyzing large datasets may help identify subgroups of patients and guide the development of more tailored intervention strategies [85]. Additionally, telehealth platforms are expected to play a key role in improving access to interventions, addressing geographical barriers, and reaching underserved populations [86].

Conclusions and prospects

Advancements in the neuroscientific understanding of chronic pain have introduced new paradigms in rehabilitation interventions. Neuroscience-based approaches such as PNE, mindfulness, and CFT directly target the neurobiological mechanisms of chronic pain, enabling more effective pain management. These interventions go beyond symptom relief, focusing on regulating central sensitization, promoting neuroplasticity, and reorganizing the pain neuromatrix to support long-term pain management and functional recovery.

A notable aspect of these approaches is their incorporation of educational components, which help reshape patients' understanding and perception of pain, leading to sustained outcomes. This highlights the importance of active patient involvement and self-management in chronic pain care. Furthermore, the integration of multiple interventions has been shown to be more effective than standalone treatments, reflecting the complex nature of chronic pain and the necessity for multifaceted strategies.

To optimize the clinical application of these interventions, further research and the development of standardized protocols are essential. The evolution of digital technologies is expected to enhance the delivery and monitoring of these interventions, making them more accessible and efficient. In conclusion, neuroscience-based interventions represent a critical milestone in the future of chronic pain management, offering a patient-centered and integrative approach that redefines the direction of rehabilitation practices.

Abbreviations

CFT: cognitive functional therapy

CNS: central nervous system

fMRI: functional magnetic resonance imaging

GMI: graded motor imagery

HPA: hypothalamic-pituitary-adrenal

PNE: Pain Neuroscience Education

Declarations

Author contributions

HK: Conceptualization, Methodology, Investigation, Resources, Writing—original draft, Writing—review & editing, Supervision. The author has read and approved the submitted version of the manuscript.

Conflicts of interest

The author declares that there are no conflicts of interest.

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Consent to participate

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References

1. Treede R, Rief W, Barke A, Aziz Q, Bennett MI, Benoliel R, et al. Chronic pain as a symptom or a disease: the IASP Classification of Chronic Pain for the International Classification of Diseases (ICD-11). Pain. 2019;160:19–27. [DOI] [PubMed]
2. Rice ASC, Smith BH, Blyth FM. Pain and the global burden of disease. Pain. 2016;157:791–6. [DOI] [PubMed]
3. Dahlhamer J, Lucas J, Zelaya C, Nahin R, Mackey S, DeBar L, et al. Prevalence of Chronic Pain and High-Impact Chronic Pain Among Adults - United States, 2016. MMWR Morb Mortal Wkly Rep. 2018;67: 1001–6. [DOI] [PubMed] [PMC]
4. Foster NE, Anema JR, Cherkin D, Chou R, Cohen SP, Gross DP, et al.; Lancet Low Back Pain Series Working Group. Prevention and treatment of low back pain: evidence, challenges, and promising directions. Lancet. 2018;391:2368–83. [DOI] [PubMed]
5. O'Sullivan PB, Caneiro JP, O'Keeffe M, Smith A, Dankaerts W, Fersum K, et al. Cognitive Functional Therapy: An Integrated Behavioral Approach for the Targeted Management of Disabling Low Back Pain. Phys Ther. 2018;98:408–23. [DOI] [PubMed] [PMC]
6. Price DD. Psychological and neural mechanisms of the affective dimension of pain. Science. 2000;288: 1769–72. [DOI] [PubMed]
7. Woolf CJ. Central sensitization: implications for the diagnosis and treatment of pain. Pain. 2011;152: S2–15. [DOI] [PubMed] [PMC]
8. Moseley GL, Butler DS. Fifteen Years of Explaining Pain: The Past, Present, and Future. J Pain. 2015;16: 807–13. [DOI] [PubMed]
9. Louw A, Zimney K, Puentedura EJ, Diener I. The efficacy of pain neuroscience education on musculoskeletal pain: A systematic review of the literature. Physiother Theory Pract. 2016;32: 332–55. [DOI] [PubMed]
10. Shin S, Kim H. Carryover Effects of Pain Neuroscience Education on Patients with Chronic Lower Back Pain: A Systematic Review and Meta-Analysis. Medicina (Kaunas). 2023;59:1268. [DOI] [PubMed] [PMC]
11. Song J, Kim H, Jung J, Lee S. Soft-Tissue Mobilization and Pain Neuroscience Education for Chronic Nonspecific Low Back Pain with Central Sensitization: A Prospective Randomized Single-Blind Controlled Trial. Biomedicines. 2023;11:1249. [DOI] [PubMed] [PMC]

12. Kim H, Lee S. The Efficacy of Pain Neuroscience Education on Active Rehabilitation Following Arthroscopic Rotator Cuff Repair: A CONSORT-Compliant Prospective Randomized Single-Blind Controlled Trial. Brain Sci. 2022;12:764. [DOI] [PubMed] [PMC]
13. Kuner R, Flor H. Structural plasticity and reorganisation in chronic pain. Nat Rev Neurosci. 2016;18: 20–30. [DOI] [PubMed]
14. Ghosh K, Pan H. Epigenetic Mechanisms of Neural Plasticity in Chronic Neuropathic Pain. ACS Chem Neurosci. 2022;13:432–41. [DOI] [PubMed]
15. Melzack R. Evolution of the neuromatrix theory of pain. The Prithvi Raj Lecture: presented at the third World Congress of World Institute of Pain, Barcelona 2004. Pain Pract. 2005;5:85–94. [DOI] [PubMed]
16. Garcia-Larrea L, Peyron R. Pain matrices and neuropathic pain matrices: a review. Pain. 2013;154: S29–43. [DOI] [PubMed]
17. Latremoliere A, Woolf CJ. Central sensitization: a generator of pain hypersensitivity by central neural plasticity. J Pain. 2009;10:895–926. [DOI] [PubMed] [PMC]
18. Meeus M, Nijs J. Central sensitization: a biopsychosocial explanation for chronic widespread pain in patients with fibromyalgia and chronic fatigue syndrome. Clin Rheumatol. 2007;26:465–73. [DOI] [PubMed] [PMC]
19. Mansour AR, Baliki MN, Huang L, Torbey S, Herrmann KM, Schnitzer TJ, et al. Brain white matter structural properties predict transition to chronic pain. Pain. 2013;154:2160–8. [DOI] [PubMed] [PMC]
20. Baliki MN, Schnitzer TJ, Bauer WR, Apkarian AV. Brain morphological signatures for chronic pain. PLoS One. 2011;6:e26010. [DOI] [PubMed] [PMC]
21. Seminowicz DA, Wideman TH, Naso L, Hatami-Khoroushahi Z, Fallatah S, Ware MA, et al. Effective treatment of chronic low back pain in humans reverses abnormal brain anatomy and function. J Neurosci. 2011;31:7540–50. [DOI] [PubMed] [PMC]
22. Edwards RR, Dworkin RH, Sullivan MD, Turk DC, Wasan AD. The Role of Psychosocial Processes in the Development and Maintenance of Chronic Pain. J Pain. 2016;17:T70–92. [DOI] [PubMed] [PMC]
23. Generaal E, Vogelzangs N, Macfarlane GJ, Geenen R, Smit JH, Geus EJCNd, et al. Biological stress systems, adverse life events and the onset of chronic multisite musculoskeletal pain: a 6-year cohort study. Ann Rheum Dis. 2016;75:847–54. [DOI] [PubMed]
24. Gil KM, Keefe FJ, Crisson JE, Dalfsen PJV. Social support and pain behavior. Pain. 1987;29:209–17. [DOI] [PubMed]
25. Krahé C, Springer A, Weinman JA, Fotopoulou A. The social modulation of pain: others as predictive signals of salience - a systematic review. Front Hum Neurosci. 2013;7:386. [DOI] [PubMed] [PMC]
26. Eisenberger NI. The pain of social disconnection: examining the shared neural underpinnings of physical and social pain. Nat Rev Neurosci. 2012;13:421–34. [DOI] [PubMed]
27. Nijs J, Torres-Cueco R, Wilgen CPv, Girbes EL, Struyf F, Roussel N, et al. Applying modern pain neuroscience in clinical practice: criteria for the classification of central sensitization pain. Pain Physician. 2014;17:447–57. [PubMed]
28. Malfliet A, Coppieters I, Wilgen PV, Kregel J, Pauw RD, Dolphens M, et al. Brain changes associated with cognitive and emotional factors in chronic pain: A systematic review. Eur J Pain. 2017;21: 769–86. [DOI] [PubMed]
29. Moseley GL. Evidence for a direct relationship between cognitive and physical change during an education intervention in people with chronic low back pain. Eur J Pain. 2004;8:39–45. [DOI] [PubMed]
30. Mills SEE, Nicolson KP, Smith BH. Chronic pain: a review of its epidemiology and associated factors in population-based studies. Br J Anaesth. 2019;123:e273–83. [DOI] [PubMed] [PMC]
31. Moseley GL, Butler DS. Explain pain supercharged. Painos Australia: Noigroup publication Liite; 2017.
32. Apkarian VA, Hashmi JA, Baliki MN. Pain and the brain: specificity and plasticity of the brain in clinical chronic pain. Pain. 2011;152:S49–64. [DOI] [PubMed] [PMC]

33. Simons LE, Moulton EA, Linnman C, Carpino E, Becerra L, Borsook D. The human amygdala and pain: evidence from neuroimaging. Hum Brain Mapp. 2014;35:527–38. [DOI] [PubMed] [PMC]
34. Craig ADB. How do you feel--now? The anterior insula and human awareness. Nat Rev Neurosci. 2009; 10:59–70. [DOI] [PubMed]
35. Tracey I, Bushnell MC. How neuroimaging studies have challenged us to rethink: is chronic pain a disease? J Pain. 2009;10:1113–20. [DOI] [PubMed]
36. Fersum KV, O'Sullivan P, Skouen JS, Smith A, Kvåle A. Efficacy of classification-based cognitive functional therapy in patients with non-specific chronic low back pain: a randomized controlled trial. Eur J Pain. 2013;17:916–28. [DOI] [PubMed] [PMC]
37. O'Sullivan P. It's time for change with the management of non-specific chronic low back pain. Br J Sports Med. 2012;46:224–7. [DOI] [PubMed]
38. Nijs J, Girbés EL, Lundberg M, Malfliet A, Sterling M. Exercise therapy for chronic musculoskeletal pain: Innovation by altering pain memories. Man Ther. 2015;20:216–20. [DOI] [PubMed]
39. Wand BM, Parkitny L, O'Connell NE, Luomajoki H, McAuley JH, Thacker M, et al. Cortical changes in chronic low back pain: current state of the art and implications for clinical practice. Man Ther. 2011; 16:15–20. [DOI] [PubMed]
40. Pelletier R, Higgins J, Bourbonnais D. Is neuroplasticity in the central nervous system the missing link to our understanding of chronic musculoskeletal disorders? BMC Musculoskelet Disord. 2015;16:25. [DOI] [PubMed] [PMC]
41. Zeidan F, Vago DR. Mindfulness meditation-based pain relief: a mechanistic account. Ann N Y Acad Sci. 2016;1373:114–27. [DOI] [PubMed] [PMC]
42. Tang Y, Hölzel BK, Posner MI. The neuroscience of mindfulness meditation. Nat Rev Neurosci. 2015; 16:213–25. [DOI] [PubMed]
43. Garland EL, Manusov EG, Froeliger B, Kelly A, Williams JM, Howard MO. Mindfulness-oriented recovery enhancement for chronic pain and prescription opioid misuse: results from an early-stage randomized controlled trial. J Consult Clin Psychol. 2014;82:448–59. [DOI] [PubMed] [PMC]
44. Brown RP, Gerbarg PL. Sudarshan Kriya yogic breathing in the treatment of stress, anxiety, and depression: part I-neurophysiologic model. J Altern Complement Med. 2005;11:189–201. [DOI] [PubMed]
45. Davidson RJ, Kabat-Zinn J, Schumacher J, Rosenkranz M, Muller D, Santorelli SF, et al. Alterations in brain and immune function produced by mindfulness meditation. Psychosom Med. 2003;65:564–70. [DOI] [PubMed]
46. Cherkin DC, Sherman KJ, Balderson BH, Cook AJ, Anderson ML, Hawkes RJ, et al. Effect of Mindfulness-Based Stress Reduction vs Cognitive Behavioral Therapy or Usual Care on Back Pain and Functional Limitations in Adults With Chronic Low Back Pain: A Randomized Clinical Trial. JAMA. 2016;315: 1240–9. [DOI] [PubMed] [PMC]
47. Mallari B, Spaeth EK, Goh H, Boyd BS. Virtual reality as an analgesic for acute and chronic pain in adults: a systematic review and meta-analysis. J Pain Res. 2019;12:2053–85. [DOI] [PubMed] [PMC]
48. Matamala-Gomez M, Donegan T, Bottiroli S, Sandrini G, Sanchez-Vives MV, Tassorelli C. Immersive Virtual Reality and Virtual Embodiment for Pain Relief. Front Hum Neurosci. 2019;13:279. [DOI] [PubMed] [PMC]
49. Gold JI, Belmont KA, Thomas DA. The neurobiology of virtual reality pain attenuation. Cyberpsychol Behav. 2007;10:536–44. [DOI] [PubMed]
50. Bowering KJ, O'Connell NE, Tabor A, Catley MJ, Leake HB, Moseley GL, et al. The effects of graded motor imagery and its components on chronic pain: a systematic review and meta-analysis. J Pain. 2013;14:3–13. [DOI] [PubMed]
51. Moseley GL. Graded motor imagery for pathologic pain: a randomized controlled trial. Neurology. 2006;67:2129–34. [DOI] [PubMed]

52. Pietro FD, McAuley JH, Parkitny L, Lotze M, Wand BM, Moseley GL, et al. Primary motor cortex function in complex regional pain syndrome: a systematic review and meta-analysis. J Pain. 2013;14: 1270–88. [DOI] [PubMed]
53. Sielski R, Rief W, Glombiewski JA. Efficacy of Biofeedback in Chronic back Pain: a Meta-Analysis. Int J Behav Med. 2017;24:25–41. [DOI] [PubMed]
54. Jensen MP, Sherlin LH, Gertz KJ, Braden AL, Kupper AE, Gianas A, et al. Brain EEG activity correlates of chronic pain in persons with spinal cord injury: clinical implications. Spinal Cord. 2013;51:55–8. [DOI] [PubMed]
55. Roy R, Vega Rdl, Jensen MP, Miró J. Neurofeedback for Pain Management: A Systematic Review. Front Neurosci. 2020;14:671. [DOI] [PubMed] [PMC]
56. Mehling WE, Wrubel J, Daubenmier JJ, Price CJ, Kerr CE, Silow T, et al. Body Awareness: a phenomenological inquiry into the common ground of mind-body therapies. Philos Ethics Humanit Med. 2011;6:6. [DOI] [PubMed] [PMC]
57. Woodman JP, Moore NR. Evidence for the effectiveness of Alexander Technique lessons in medical and health-related conditions: a systematic review. Int J Clin Pract. 2012;66:98–112. [DOI] [PubMed]
58. Mehling WE, Gopisetty V, Daubenmier J, Price CJ, Hecht FM, Stewart A. Body awareness: construct and self-report measures. PLoS One. 2009;4:e5614. [DOI] [PubMed] [PMC]
59. Nijs J, Wijma AJ, Willaert W, Huysmans E, Mintken P, Smeets R, et al. Integrating Motivational Interviewing in Pain Neuroscience Education for People With Chronic Pain: A Practical Guide for Clinicians. Phys Ther. 2020;100:846–59. [DOI] [PubMed]
60. Malfliet A, Kregel J, Coppieters I, Pauw RD, Meeus M, Roussel N, et al. Effect of Pain Neuroscience Education Combined With Cognition-Targeted Motor Control Training on Chronic Spinal Pain: A Randomized Clinical Trial. JAMA Neurol. 2018;75:808–17. [DOI] [PubMed] [PMC]
61. Hilton L, Hempel S, Ewing BA, Apaydin E, Xenakis L, Newberry S, et al. Mindfulness Meditation for Chronic Pain: Systematic Review and Meta-analysis. Ann Behav Med. 2017;51:199–213. [DOI] [PubMed] [PMC]
62. Smart KM, Blake C, Staines A, Thacker M, Doody C. Mechanisms-based classifications of musculoskeletal pain: part 1 of 3: symptoms and signs of central sensitisation in patients with low back (± leg) pain. Man Ther. 2012;17:336–44. [DOI] [PubMed]
63. Wijma AJ, Wilgen CPv, Meeus M, Nijs J. Clinical biopsychosocial physiotherapy assessment of patients with chronic pain: The first step in pain neuroscience education. Physiother Theory Pract. 2016;32: 368–84. [DOI] [PubMed]
64. Hill JC, Whitehurst DGT, Lewis M, Bryan S, Dunn KM, Foster NE, et al. Comparison of stratified primary care management for low back pain with current best practice (STarT Back): a randomised controlled trial. Lancet. 2011;378:1560–71. [DOI] [PubMed] [PMC]
65. Nicholas MK, Costa DSJ, Linton SJ, Main CJ, Shaw WS, Pearce G, et al. Implementation of Early Intervention Protocol in Australia for “High Risk” Injured Workers is Associated with Fewer Lost Work Days Over 2 Years Than Usual (Stepped) Care. J Occup Rehabil. 2020;30:93–104. [DOI] [PubMed]
66. Côté P, Wong JJ, Sutton D, Shearer HM, Mior S, Randhawa K, et al. Management of neck pain and associated disorders: A clinical practice guideline from the Ontario Protocol for Traffic Injury Management (OPTIMa) Collaboration. Eur Spine J. 2016;25:2000–22. [DOI] [PubMed]
67. Edwards RR, Dworkin RH, Turk DC, Angst MS, Dionne R, Freeman R, et al. Patient phenotyping in clinical trials of chronic pain treatments: IMMPACT recommendations. Pain. 2016;157:1851–71. [DOI] [PubMed] [PMC]
68. Caneiro JP, Smith A, Rabey M, Moseley GL, O’Sullivan P. Process of Change in Pain-Related Fear: Clinical Insights From a Single Case Report of Persistent Back Pain Managed With Cognitive Functional Therapy. J Orthop Sports Phys Ther. 2017;47:637–51. [DOI] [PubMed]

69. Andronis L, Kinghorn P, Qiao S, Whitehurst DGT, Durrell S, McLeod H. Cost-Effectiveness of Non-Invasive and Non-Pharmacological Interventions for Low Back Pain: a Systematic Literature Review. Appl Health Econ Health Policy. 2017;15:173–201. [DOI] [PubMed]
70. Dear BF, Zou JB, Ali S, Lorian CN, Johnston L, Sheehan J, et al. Clinical and cost-effectiveness of therapist-guided internet-delivered cognitive behavior therapy for older adults with symptoms of anxiety: a randomized controlled trial. Behav Ther. 2015;46:206–17. [DOI] [PubMed]
71. Hill JC, Garvin S, Chen Y, Cooper V, Wathall S, Saunders B, et al. Stratified primary care versus non-stratified care for musculoskeletal pain: findings from the STarT MSK feasibility and pilot cluster randomized controlled trial. BMC Fam Pract. 2020;21:30. [DOI] [PubMed] [PMC]
72. Dworkin RH, Turk DC, Farrar JT, Haythornthwaite JA, Jensen MP, Katz NP, et al. Core outcome measures for chronic pain clinical trials: IMMPACT recommendations. Pain. 2005;113:9–19. [DOI] [PubMed]
73. Chiarotto A, Boers M, Deyo RA, Buchbinder R, Corbin TP, Costa LOP, et al. Core outcome measurement instruments for clinical trials in nonspecific low back pain. Pain. 2018;159:481–95. [DOI] [PubMed] [PMC]
74. Vlaeyen JWS, Morley S, Crombez G. The experimental analysis of the interruptive, interfering, and identity-distorting effects of chronic pain. Behav Res Ther. 2016;86:23–34. [DOI] [PubMed]
75. Tracey I, Mantyh PW. The cerebral signature for pain perception and its modulation. Neuron. 2007;55:377–91. [DOI] [PubMed]
76. Lin I, Wiles L, Waller R, Goucke R, Nagree Y, Gibberd M, et al. What does best practice care for musculoskeletal pain look like? Eleven consistent recommendations from high-quality clinical practice guidelines: systematic review. Br J Sports Med. 2020;54:79–86. [DOI] [PubMed]
77. Becker WC, Dorflinger L, Edmond SN, Islam L, Heapy AA, Fraenkel L. Barriers and facilitators to use of non-pharmacological treatments in chronic pain. BMC Fam Pract. 2017;18:41. [DOI] [PubMed] [PMC]
78. Moseley GL. Teaching people about pain: why do we keep beating around the bush? Pain Manag. 2012;2:1–3. [DOI] [PubMed]
79. Malloy KM, Milling LS. The effectiveness of virtual reality distraction for pain reduction: a systematic review. Clin Psychol Rev. 2010;30:1011–8. [DOI] [PubMed]
80. Li Y, Chung TY, Lu W, Li M, Ho YWB, He M, et al. Chatbot-Based Mindfulness-Based Stress Reduction Program for University Students With Depressive Symptoms: Intervention Development and Pilot Evaluation. J Am Psychiatr Nurses Assoc. 2024;[Epub ahead of print]. [DOI] [PubMed]
81. Cascella M, Cascella A, Monaco F, Shariff MN. Envisioning gamification in anesthesia, pain management, and critical care: basic principles, integration of artificial intelligence, and simulation strategies. J Anesth Analg Crit Care. 2023;3:33. [DOI] [PubMed] [PMC]
82. Lalloo C, Jibb LA, Rivera J, Agarwal A, Stinson JN. "There's a Pain App for That": Review of Patient-targeted Smartphone Applications for Pain Management. Clin J Pain. 2015;31:557–63. [DOI] [PubMed]
83. Thacker MA, Moseley GL. First-person neuroscience and the understanding of pain. Med J Aust. 2012;196:410–1. [DOI] [PubMed]
84. Mitsea E, Drigas A, Skianis C. Digitally Assisted Mindfulness in Training Self-Regulation Skills for Sustainable Mental Health: A Systematic Review. Behav Sci (Basel). 2023;13:1008. [DOI] [PubMed] [PMC]
85. Keefe FJ, Huling DA, Coggins MJ, Keefe DF, Rosenthal ZM, Herr NR, et al. Virtual reality for persistent pain: a new direction for behavioral pain management. Pain. 2012;153:2163–6. [DOI] [PubMed] [PMC]
86. Kroenke K, Krebs EE, Wu J, Yu Z, Chumbler NR, Bair MJ. Telecare collaborative management of chronic pain in primary care: a randomized clinical trial. JAMA. 2014;312:240–8. [DOI] [PubMed]