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Research Article

Exercise-Induced Hypoalgesia: Mechanisms, Clinical Evidence, And Implications For Chronic Pain Management.

Gen Li[a†], Xuewan Lin[a†], Zheng Wang[b], Songtao Wang[a*]

[a]*School of Physical Education & Sports Science, South China Normal University, Guangzhou, 510006, China.*
[b]*Department of Nuclear Medicine, The First Affiliated Hospital of Jinan University, Guangzhou, 510632, China.*
[†]*These authors have contributed equally to this work.*

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Abstract

Background: Chronic pain affects over 20% of adults worldwide, and traditional pharmacological treatments have limitations in efficacy and safety concerns. Exercise-induced hypoalgesia (EIH), as a non-pharmacological analgesic mechanism, demonstrates broad application prospects in chronic pain management. This review aims to systematically summarize the neurobiological mechanisms, clinical evidence, and practical application strategies of EIH.
Methods: This review synthesizes current evidence on EIH mechanisms across central, peripheral, and psychosocial domains, and examines clinical findings in patients with chronic pain conditions, including low back pain, osteoarthritis, chronic neck pain, and fibromyalgia.
Results: EIH involves coordinated activation of descending pain inhibitory pathways, release of endogenous opioids and monoaminergic neurotransmitters, peripheral immune modulation through myokine secretion, and psychosocial factors including expectancy, pain catastrophizing, and kinesiophobia. In chronic pain patients, structured exercise interventions demonstrate analgesic effects, though responses exhibit significant disease-specificity and individual variability. Notably, patients with central sensitization syndromes may exhibit attenuated or paradoxical hyperalgesic responses to exercise.
Conclusions: EIH is a multidimensional phenomenon integrating physiological and psychological mechanisms. Clinical application requires individualized exercise prescription encompassing modality, intensity, duration, and frequency, combined with multimodal integration and patient stratification based on pain phenotype and endogenous pain modulation capacity. Future research should prioritize development of predictive biomarkers for EIH, longitudinal outcome studies, and mechanistic investigations in refractory pain populations to advance precision exercise-based pain management.
Perspective: This review synthesizes neurophysiological and psychological mechanisms underlying exercise-induced hypoalgesia and its clinical applications in chronic pain management. Understanding how exercise modulates pain through central and peripheral pathways can guide clinicians in designing personalized, evidence-based exercise interventions to optimize analgesic outcomes while minimizing risks of exercise-induced hyperalgesia in vulnerable populations.

Keywords: Exercise-induced hypoalgesia; Chronic pain; Pain modulation; Descending pain modulation; Exercise prescription

***Corresponding Author:** **Songtao Wang, Ph.D.** School of Physical Education & Sports Science South China Normal University,China.
Email: wangsongtao@m.scnu.edu.cn.
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INTRODUCTION

Chronic pain represents a complex and persistent health problem that profoundly impacts patients' quality of life, physical function, and social productivity. Global epidemiological data indicate that the prevalence of chronic pain exceeds 20% in the adult population, with primary etiologies encompassing musculoskeletal disorders, neuropathic pain syndromes, and widespread pain disorders[1]. However, chronic pain management continues to face substantial challenges. Pharmacological treatments, particularly opioid medications, demonstrate significant limitations in long-term efficacy, tolerability, and safety, accompanied by risks of dependence and abuse[2]. Consequently, non-pharmacological treatment strategies have garnered increasing attention, with exercise interventions recognized as a promising therapeutic approach due to their high accessibility, minimal side effects, and capacity to deliver multidimensional health benefits[3].

Exercise-induced hypoalgesia (EIH) refers to the phenomenon of acute reduction in pain perception following a single bout of exercise. This phenomenon was first described in the 1970s in aerobic exercise studies with healthy populations and has since been reported across diverse exercise types, intensities, and populations[4]. Recent research has increasingly recognized that EIH is not merely a transient post-exercise analgesic response but may also promote long-term adaptation of endogenous analgesic mechanisms through repeated induction via structured exercise programs, thereby exerting sustained effects in chronic pain management[5, 6].

However, EIH manifestations exhibit significant variability across populations. In healthy individuals, EIH responses are stable and robust; conversely, in chronic pain populations, particularly in conditions characterized by central sensitization, EIH responses demonstrate greater fluctuation, with some patients even exhibiting exercise-induced hyperalgesia and short-term symptom exacerbation[7, 8]. This phenomenon suggests that clinical exercise prescription should carefully consider dose-response relationships and exercise modalities, adopt individualized intervention strategies, and address psychological modulatory factors such as emotion, expectancy, and catastrophizing to minimize risks of symptom aggravation and enhance adherence and efficacy.

Furthermore, existing research exhibits methodological limitations: heterogeneity across studies in exercise protocols, pain assessment methods, and participant characteristics compromises result comparability; most trials employ small sample sizes, and studies examining long-term persistence of EIH effects remain limited; mechanistic research predominantly involves healthy populations, necessitating cautious interpretation when extrapolating to chronic pain patients. In summary, this review aims to systematically summarize recent advances in the neurobiological mechanisms, clinical evidence, and practical implications of EIH in chronic pain management, and to explore current research limitations and future directions, with the goal of advancing EIH toward mechanism-interpretable, prescription-executable, evidence-based pain management strategies.

2. PHYSIOLOGICAL AND PSYCHOLOGICAL MECHANISMS OF EXERCISE-INDUCED HYPOALGESIA

2.1 Central Nervous System Regulatory Mechanisms

One of the core mechanisms underlying exercise-induced hypoalgesia (EIH) is the descending pain inhibitory action of the central nervous system. The descending inhibitory pathway comprises a multi-level structure consisting of the periaqueductal gray (PAG), rostral ventromedial medulla (RVM), and spinal dorsal horn (DH), constituting an important defensive system for modulating nociceptive signals[9]. During acute exercise, the PAG receives multimodal inputs from motor cortex, limbic system, and brainstem, and drives inhibitory interneurons in the spinal dorsal horn via the RVM, reducing afferent signals from Aδ and C fibers, thereby elevating pain threshold[10]. During this process, release of monoaminergic neurotransmitters such as noradrenaline (NA) and serotonin (5-HT) is significantly enhanced, executing analgesic functions through α2-adrenergic receptors and 5-HT1/5-HT3 receptors, respectively[11]. Additionally, exercise activates the endogenous opioid system, including multiple peptides such as β-endorphin, enkephalins, and dynorphins. These molecules directly bind to μ, δ, and κ opioid receptors in the spinal cord and brain, inhibiting transmission of pain signals[4]. Studies employing opioid receptor antagonists to block the central opioid system have observed significant attenuation of exercise-related pain threshold elevation, further confirming the critical role of opioidergic pathways in central analgesia[12].

Neuroimaging studies provide direct evidence for the aforementioned central mechanisms. Functional magnetic resonance imaging (fMRI) studies demonstrate that exercise induces enhanced activity in the PAG, RVM, and anterior cingulate cortex (ACC), with significant elevation of functional connectivity associated with pain inhibition[13]. Concurrently, key nodes of pain pathways such as the insula and primary somatosensory cortex (S1) exhibit decreased activity following exercise, suggesting that pain signals are reweighted and inhibited at the central level[14]. Resting-state functional connectivity analysis further reveals increased connectivity between the PAG and prefrontal cortex post-exercise, potentially reflecting enhanced cognitive modulation of pain experience by the prefrontal cortex under exercise induction[15]. Furthermore, brain chemical imaging techniques (such as magnetic resonance spectroscopy, MRS) have confirmed that post-exercise changes in the ratio

of glutamate to γ-aminobutyric acid (GABA) in the brain demonstrate significant correlation with pain inhibitory effects[16]. This multimodal evidence collectively reveals the central basis of EIH: through activation of descending pain inhibitory systems, modulation of neurotransmitter release, and enhancement of functional connectivity in pain-related brain regions, exercise can significantly reshape central pain processing networks within a short timeframe, achieving analgesic effects.

2.2 Peripheral Mechanisms and Immune Modulation

Beyond the action of central descending analgesic systems, EIH also relies on synergistic participation of peripheral mechanisms, particularly metabolic and immune responses generated during skeletal muscle contraction, which can directly or indirectly reduce peripheral nociceptor sensitivity.

Skeletal muscle releases various myokines during exercise, including interleukin-6 (IL-6), brain-derived neurotrophic factor (BDNF), and lactate[17]. IL-6 exhibits acute elevation post-exercise, primarily mediating anti-inflammatory rather than pro-inflammatory responses by suppressing expression of pro-inflammatory cytokines such as tumor necrosis factor-α (TNF-α) and interleukin-1β (IL-1β)[18]. Concurrently, BDNF modulates nociception at multiple sites in the periphery and spinal cord through TrkB-mediated PLCγ/PI3K/MAPK pathways, capable of both pro-nociceptive and anti-nociceptive actions, with the latter predominating within the overall exercise-induced network to promote pain inhibition and tissue repair[19]. Additionally, muscle activity significantly increases local and systemic blood flow, facilitating clearance of metabolic products such as lactate, prostaglandins, ATP, and acidic ions. Accumulation of these products in muscle or joint tissues can persistently stimulate nociceptors and provoke pain[20]. Therefore, the immediate peripheral effects of exercise include improved tissue oxygenation, optimized metabolic environment, and reduced inflammatory sources through myokine-mediated immune regulation, thereby attenuating peripheral sensitization.

Immune modulation occupies an important position in the peripheral mechanisms of EIH. Chronic pain patients commonly exhibit low-grade systemic inflammatory states, which not only maintain peripheral sensitization but also further promote central sensitization through increased nociceptive input[21]. Exercise intervention, particularly moderate-intensity aerobic training, can suppress monocyte release of pro-inflammatory cytokines (such as TNF-α and IL-1β) while elevating levels of anti-inflammatory cytokines (such as IL-10)[18]. This pro-anti-inflammatory immune shift can downregulate nociceptor firing frequency and reduce the inflammatory environment in local tissues, thereby attenuating generation of pain signals[22]. Furthermore, exercise can influence peripheral nerve ion channel function, such as reducing expression of TRPV1 receptors and Nav1.8 sodium channels, which are highly associated with peripheral sensitization[23].

Exercise can also synergistically improve circulation and immune homeostasis through remodeling of autonomic nervous activity. On one hand, regular aerobic training attenuates noradrenaline-mediated vasoconstriction responses in active muscles, thereby enhancing local perfusion and optimizing peripheral circulation[24]; on the other hand, exercise-induced adrenaline regulates immune cell mobilization and activation states through β-receptors, promoting anti-inflammatory phenotype and functional remodeling[25], thereby improving systemic and local inflammatory microenvironments.

In summary, peripheral metabolic improvement and immune modulation not only serve as important complements to central mechanisms but also provide crucial biological foundations for individualized application of EIH in chronic pain patients.

2.3 Psychosocial Mechanisms

The analgesic magnitude of EIH depends not only on central and peripheral physiological mechanisms but is also significantly modulated by psychological and social factors. Pain is a complex experience influenced by cognition, emotion, and expectancy; psychosocial variables can not only alter baseline levels of pain perception but also influence individual response patterns to exercise stimuli.

Exercise expectancy exerts an important amplification effect in EIH, with mechanisms closely related to placebo-like responses. Eippert et al.[26] demonstrated using functional imaging and naloxone blockade experiments that positive expectancy can activate the endogenous opioid system and promote coordinated activation of descending pain inhibitory pathways such as PAG and RVM, thereby significantly reducing pain perception. This psychological-neural interactive effect suggests that EIH analgesic intensity depends not only on physiological mechanisms but is also modulated by cognitive and emotional states[27]. Therefore, appropriately guiding and optimizing patient expectancy when designing exercise programs may help enhance intervention efficacy.

Pain catastrophizing represents an important negative psychological factor influencing EIH, referring to excessive threat-based interpretation and attentional bias toward pain. Catastrophizing influences pain outcomes through multiple pathways: on one hand, it enhances pain-related fear and negative emotions, promoting avoidance behaviors and activity limitation, thereby aggravating functional disability; on the other hand, it is associated with physiological responses such as sympathetic arousal, muscle tension, and inflammation, potentially weakening endogenous descending inhibition and thereby maintaining pain chronification

processes[28, 29], making it more difficult to produce analgesic responses after exercise.

Kinesiophobia also represents an important psychological barrier limiting EIH effects. Driven by pain-related fear, chronic pain patients often excessively worry that exercise may cause injury or pain exacerbation, thereby actively reducing physical activity and exercise intensity[30]. This exercise avoidance behavior not only leads to physical deconditioning but also results in insufficient exercise stimulation to trigger effective EIH responses, forming a vicious cycle of "pain-fear-avoidance." Conversely, higher self-efficacy is not only associated with stronger pain tolerance and lower functional limitations but can also promote exercise confidence and adherence[31]. By maintaining adequate exercise volume and intensity, self-efficacy facilitates full activation of peripheral and central analgesic mechanisms, thereby enhancing EIH effects.

Conditioned pain modulation (CPM) is a commonly used paradigm for assessing individual endogenous pain inhibitory capacity. Research indicates that the magnitude of CPM inhibition correlates to some extent with EIH response patterns, with individuals exhibiting stronger CPM effects often also demonstrating more pronounced EIH[32]. However, this correlation is not entirely consistent, as the two differ in physiological mechanisms, individual variability, and effect duration[33]. Some chronic pain patients exhibit normal CPM responses but markedly insufficient post-exercise EIH responses, suggesting that EIH may involve psychological-cognitive components distinct from classical CPM.

Attentional modulation plays an important role in exercise-induced analgesia. When individuals shift attention from pain sensations to the exercise task itself during exercise, excessive activation of pain-related brain regions (such as the insula and ACC) is significantly attenuated, while prefrontal cortex regulatory function over pain emotion is enhanced. This process not only weakens pain perception and emotional responses but can also strengthen endogenous pain inhibitory mechanisms through activation of descending analgesic networks[34]. Additionally, emotional state represents an important factor influencing EIH, with positive emotions (such as pleasure and satisfaction) commonly associated with enhanced analgesic responses, while negative emotions such as anxiety and depression weaken EIH effects[15]. As an important variable modulating psychological mechanisms, social support can enhance patients' exercise motivation and persistence, thereby indirectly amplifying EIH effects[35].

In summary, psychosocial mechanisms can both directly influence EIH occurrence through modulation of central pain networks and determine analgesic response magnitude through shaping exercise behavioral patterns. Their role is particularly important in individualized exercise management of chronic pain patients.

3. DOSE-RESPONSE RELATIONSHIPS OF EXERCISE-INDUCED HYPOALGESIA

3.1 Exercise Modality

Different exercise modalities exhibit significant variations in their capacity to induce EIH. Aerobic exercise, through sustained muscle contraction and cardiopulmonary system loading, promotes release of endogenous opioids and monoaminergic neurotransmitters, thereby enhancing inhibitory effects of the PAG-RVM pathway[36]. Resistance exercise produces both central and peripheral analgesic effects through metabolic stimulation and myokine secretion generated by localized muscle contraction[36]. In comparison, high-intensity interval training (HIIT), due to its intense metabolic load and acute stress response, may produce more transient but higher-peak EIH, suitable for selected individuals with good tolerance[37]. On the other hand, low-intensity activities such as yoga and Tai Chi demonstrate relatively weaker EIH effects, with analgesic mechanisms primarily dependent on psychological regulation and optimization of autonomic nervous balance; however, they possess unique value in improving psychological status and enhancing exercise adherence in chronic pain patients[38]. Furthermore, exercise modalities exhibit differential EIH induction efficacy across chronic pain subtypes, as detailed in Section 4.

3.2 Exercise Intensity

Exercise intensity represents a critical dose factor influencing EIH magnitude. Moderate to moderately high-intensity aerobic exercise (60–75% VO_2max or 60–75% maximum heart rate) has been consistently demonstrated by substantial research to reliably induce significant EIH, whereas low-intensity exercise (<50% maximum heart rate) often fails to achieve significant analgesic effects[4].High-intensity resistance training involving large muscle groups is superior to small muscle group training in inducing analgesia, potentially related to greater β-endorphin release from the pituitary stimulated by large muscle contraction, subsequently activating descending pain inhibitory pathways[39]. Excessively low intensity often fails to reach the intensity/duration threshold required to induce EIH[40], while excessively high intensity (particularly involving substantial eccentric components or novel, high-load training) readily triggers post-exercise muscle damage and delayed-onset muscle soreness (DOMS), with short-term increases in pain sensitivity, termed exercise-induced hyperalgesia[41]. This phenomenon is particularly prominent in chronic pain patients, especially in conditions characterized by central sensitization, where some high-load or rapidly progressive protocols may lead to short-term symptom exacerbation, suggesting that intensity prescription should adopt cautious, progressive strategies. Additionally, individual psychological status can significantly modulate adaptation and response

to intensity. Therefore, exercise intensity prescription should integrate both physiological and psychological perspectives, with individualized adjustments based on patients' baseline function, pain sensitivity, and psychological characteristics, to adequately activate analgesic mechanisms while avoiding risks of hyperalgesia[42].

3.3 Duration of EIH Effects

As an acute response, the analgesic effect of EIH is influenced by exercise modality, intensity, and individual differences, typically manifesting and gradually dissipating within minutes to hours following exercise cessation[43]. Aerobic exercise typically produces analgesic effects immediately post-exercise, gradually diminishing over tens of minutes to several hours; the analgesic effect of resistance training sometimes appears with a delay of several minutes and demonstrates relatively shorter duration[5];high-intensity interval training (HIIT),due to its brief but intense metabolic and nervous system loading, can elicit more pronounced analgesic responses in some healthy populations[37]. The duration of EIH in chronic pain patients is often shorter than in healthy individuals and is readily influenced by psychological factors[7]. Furthermore, delayed-onset muscle soreness (DOMS) may in some circumstances mask or attenuate EIH effects, particularly following high-intensity or novel exercise[41].Notably, repeated structured exercise training programs can enhance the persistence and magnitude of EIH responses through long-term plasticity of central analgesic pathways, thereby producing cumulative analgesic effects on chronic pain[44].

In summary, clarifying the influence patterns of different exercise modalities and intensities on EIH, as well as the dynamic persistence characteristics of analgesic effects, is crucial for optimizing exercise prescriptions for chronic pain patients and enhancing clinical efficacy of exercise therapy. Future research further integrating physiological biomarkers and psychological modulatory factors holds promise for advancing individualized precision exercise treatment.

4. CLINICAL EVIDENCE FOR EXERCISE-INDUCED HYPOALGESIA

In chronic pain populations, EIH responses demonstrate greater complexity and diversity, exhibiting pronounced disease-specificity and individual variability. Overall, structured exercise interventions can effectively alleviate symptoms and improve daily function across multiple chronic pain conditions. Evidence-based data support selection of individualized exercise programs based on patient status to relieve pain, improve function, and reduce recurrence risk.

4.1 Chronic Low Back Pain

Substantial evidence from randomized controlled trials and prospective studies demonstrates that structured exercise interventions can improve pain, function, and quality of life in patients with chronic or recurrent low back pain, though analgesic magnitude and persistence vary across exercise modalities. Behavioral therapy combined with exercise can improve psychological and functional status in chronic low back pain patients across multiple dimensions[45]. Motor control training focused on lumbo-pelvic deep muscle activation demonstrates medium- to long-term effects in reducing pain and functional disability[46]. Graded aerobic and functional training can improve symptoms in recurrent low back pain at 6–36 month follow-up[47]. Spinal stabilization training tailored to pain grade and balance differences can enhance postural control and function[48]. Multiple trials have examined the value of Pilates in chronic low back pain management, with results showing it can alleviate pain and improve function and quality of life[49-51]. Strength training studies indicate that lumbar strengthening can simultaneously improve physiological and psychological indicators[52]. Other types of rehabilitative exercise also demonstrate efficacy, such as Mensendieck somatocognitive therapy reducing symptoms of recurrent low back pain at 12 months[53].

4.2 Osteoarthritis

Substantial high-quality randomized controlled trials consistently confirm that structured exercise interventions can significantly alleviate pain, improve function and quality of life, and demonstrate good safety in patients with knee or hip osteoarthritis. Different forms of aerobic activity, including group cycling[54], walking[55], and Baduanjin[56], can all reduce pain-related disability levels. Aquatic exercise demonstrates stable analgesic and functional improvement effects across multiple trials[57-59], and improves flexibility, muscle strength, and cardiopulmonary function[60, 61]. Traditional and mind-body integrated exercises such as Tai Chi[58, 62] also demonstrate effective pain reduction and physical function improvement. Strength training and proprioceptive training similarly play important roles in knee osteoarthritis analgesia and functional improvement[63, 64], with some studies showing combined effects superior to single interventions.

The landmark FAST study demonstrated that both aerobic and resistance training were superior to health education for improving knee osteoarthritis pain and function[65]. Additionally, exercise therapy for hip osteoarthritis has demonstrated significant efficacy across multiple studies[66-69].

4.3 Chronic Neck Pain

Multiple randomized controlled trials confirm that structured exercise interventions have significant analgesic and functional recovery effects for chronic neck pain with

neurogenic components. Functional postural training targeting deep cervical flexors can improve neuromuscular coordination and cervical stability, thereby reducing pain originating from cervical nerve irritation[70]; therapeutic neck exercise combined with sleep support can reduce pain and improve functional mobility[71]; Viljanen et al.[72] compared dynamic muscle training, relaxation training, and ordinary daily activities for chronic neck pain patients, with results showing no significant differences in neck pain severity among the three groups, but patients receiving dynamic muscle training and relaxation training demonstrated greater improvements in cervical rotation and lateral flexion range of motion. Additionally, qigong and conventional exercise can both stably alleviate chronic neck pain and improve quality of life across different populations[73, 74], while group neck gymnastics can significantly reduce neck pain incidence in workplace settings[75]. This evidence collectively supports the important clinical value of regular, targeted exercise training in improving neurogenic pain symptoms, enhancing cervical function, and improving quality of life.

4.4 Fibromyalgia Syndrome

Randomized controlled trials and prospective studies consistently report that in fibromyalgia syndrome patients, structured exercise interventions (including aerobic, strength, and aquatic exercise) can typically reduce pain intensity and improve function, quality of life, and certain cognitive and neuromuscular indicators. Land-based aerobic training, whether employing short segmented or longer duration protocols, can produce beneficial changes in symptoms and physical fitness[76]; combining exercise with biofeedback/relaxation can further improve symptom and psychological outcomes[77]. Studies comparing aerobic exercise with paroxetine suggest clinical potential of non-pharmacological exercise programs in pain management[78]. Multiple randomized controlled studies of aquatic/warm water exercise repeatedly demonstrate pain reduction accompanied by improvements in lower extremity muscle strength, quality of life, and even cognitive function[79-81]. Additionally, strength training can induce significant neuromuscular functional adaptations, further confirming that fibromyalgia syndrome pathological mechanisms are primarily central rather than peripheral[82]. Synthesizing the above evidence, it is recommended to incorporate individualized, progressive aerobic, strength, and/or aquatic exercise into multidisciplinary management of fibromyalgia, with the goal of improving function and quality of life while reducing pain.

The above clinical evidence demonstrates that while EIH exhibits disease-specificity and individual variability in chronic pain patients, multiple forms of structured exercise interventions have been proven to produce analgesic effects and improve function across different chronic pain populations, providing a solid evidence-based foundation for exercise therapy as a core component of chronic pain management.

5. CLINICAL APPLICATION AND PRACTICE RECOMMENDATIONS

Exercise prescription development should be based on existing research evidence, fully considering core elements such as exercise type, frequency, duration, and intensity. Regarding exercise type, aerobic exercise (such as running, cycling, swimming) has been confirmed by substantial research to stably induce short-term analgesic effects[83]; resistance training can also produce significant analgesic effects under specific intensities with large muscle group participation[84]; mind-body integrated exercises (such as yoga, Tai Chi) may simultaneously act on psychological regulation and somatic analgesic systems[38]. Regarding exercise frequency, it is recommended that chronic pain patients initially perform moderate-intensity exercise 2–3 times per week, gradually increasing to 4–5 times per week, with dynamic adjustments based on patient adaptation responses[44]. Regarding duration, moderate- to high-intensity exercise generally can stably induce EIH within the 20–45 minute range[85]. Exercise intensity selection should be based on patients' current physical fitness and pain tolerance, typically recommended to start from 50–60% VO_2max or equivalent to 60–70% of maximum heart rate, gradually increasing load[86].

Combining exercise with other intervention measures represents an important strategy for enhancing EIH clinical efficacy. Multimodal interventions can achieve mechanistic complementarity; research demonstrates that adding manual therapy, breathing training, or mindfulness meditation to exercise training can further modulate pain-related central networks and enhance analgesic magnitude[87, 88]. These combination interventions are particularly suitable for chronic pain patients, as single exercise modalities sometimes are insufficient to overcome the dual barriers of central sensitization and psychological factors.

In summary, clinical application of EIH is not merely "prescribing exercise to patients" but requires multidimensional strategies based on scientific evidence, psychological-behavioral interventions, and individualized assessment. Through rational design of exercise prescriptions, combination of multimodal intervention approaches, and full consideration of patient differential responses, EIH holds promise to become a predictable, patronizable, and sustainable non-pharmacological analgesic core tool in chronic pain management.

6. Limitations and Future Research Directions

Existing research exhibits limitations including large sample heterogeneity, insufficient long-term follow-up, and mechanistic studies predominantly based on healthy populations. Future research needs to conduct large-sample prospective studies evaluating long-term efficacy of EIH, integrate multimodal biomarkers (neuroimaging, inflammatory markers, psychological scales) to construct predictive models, deeply elucidate pathophysiological mechanisms of EIH failure in central sensitization patients, and explore clinical value of novel exercise modalities (such as virtual reality training), to advance EIH toward precision, executable, evidence-based pain management strategies.

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