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Physical exercise as non-pharmacological treatment of chronic pain: Why and when

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Abstract

Chronic pain broadly encompasses both objectively defined conditions and idiopathic conditions that lack physical findings. Despite variance in origin or pathogenesis, these conditions are similarly characterized by chronic pain, poor physical function, mobility limitations, depression, anxiety and sleep disturbance and are treated alone or in combination by pharmacologic and nonpharmacologic approaches, such as physical activity (aerobic conditioning, muscle strengthening, flexibility training and movement therapies). Physical activity improves general health, disease risk and progression of chronic illnesses such as cardiovascular disease, type-2 diabetes and obesity. When applied to chronic pain conditions within appropriate parameters (frequency, duration, intensity), physical activity significantly improves pain and related symptoms. For chronic pain, strict guidelines for physical activity are lacking, but frequent movement is preferable to sedentary behavior. This gives considerable freedom in prescribing physical activity treatments, which are most successful when tailored individually, progressed slowly and account for physical limitations, psychosocial needs and available resources.

Keywords

chronic widespread pain; fibromyalgia; arthritis; non-pharmacological treatment; chronic pain; exercise; strength; aerobic

Introduction

Chronic pain conditions can be identified as having an: 1) objective pathogenic, genetic, or biologic origin that explains symptom presentation, or 2) idiopathic source with unknown origin for the illness. The former includes arthritis (osteoarthritis [OA], rheumatoid arthritis [RA]), systemic inflammatory rheumatic diseases, connective tissue diseases, post-herpetic

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neuralgia, and peripheral neuropathy, which are typically diagnosed via objective biologic or inflammatory markers, radiologic evidence or other identifiable tissue damage. Idiopathic conditions, which often rely on subjective patient report, include complex regional pain syndrome (CRPS), fibromyalgia (FM), chronic widespread pain (CWP), subsets of chronic low back pain (LBP), and chronic pelvic pain (CPP). These syndromes are defined by unremitting pain and may include secondary issues of fatigue, sleep disturbance, cognitive deficits and depression.(1) For this chapter, we will largely focus on arthritis and FM as prototypical chronic pain conditions of known and unknown origin, respectively. Both are incurable, challenging to treat, tend to have poor long-term prognosis and impose substantial economic burden on healthcare systems and society.

Chronic pain is a significant public health concern that differentially burdens vulnerable populations, such as the elderly, children, and ethnic/racial minorities, due to disparities in treatment and resources.(2) Recent estimates suggest that chronic pain affects 100 million people in the United States (US) and 1.5 billion people worldwide, figures that are steadily rising. (3, 4) In 2010, estimated annual costs related to chronic pain were \$560-635 billion in combined medical costs, lost earnings, disability and lost productivity. (4) Arthritis, specifically, is the leading cause of disability in the US. Combined medical costs and lost earnings exceed \$189 billion annually.(5) Arthritis is highly prevalent, affecting at least 22% of adults and nearly half of adults older than 65. Furthermore, 43.2% of those with arthritis have an arthritis-attributable activity limitation, (6) and 24-58% of adults with arthritis are physically inactive;(7-13) estimates may be low because they are primarily based on self-report measures.

Physical inactivity is an added insult to chronic pain conditions; in fact, it may contribute to the rise in chronic diseases. World Health Organization and the Centers for Disease Control and Prevention (CDC) target insufficient physical activity as a leading risk factor for noncommunicable diseases and death worldwide.(14, 15) Physical inactivity or sedentary behavior is ubiquitous at all ages, rendering many chronic diseases once relegated to older populations increasingly common in younger age groups.(16, 17) Sedentary behavior is detrimental to health, physical function and health-related quality of life.(18-21) In a nationally representative study of 2286 adults 60+ years old, each additional daily hour of sedentary behavior resulted in a 46% greater odds of disability with activities of daily living, controlling for moderate-vigorous physical activity, socioeconomic factors and health conditions.(18) Results from this study and other studies of sedentary behavior (19-21) suggest that even bursts of moderate-vigorous physical activity may not negate the harms of long, continuous hours of sedentary behavior. Regular physical activity emerges as a significant tool for both primary and secondary prevention of chronic disease with the ability to mitigate symptoms and slow or stall disease progression.(15, 16)

Usual treatments for chronic pain conditions: Poor to modest efficacy

Evidence for the effect of exercise on disease pathogenesis for chronic pain is lacking, with current evidence largely focusing on symptomatology. With no cure for many chronic pain conditions, treatments address symptoms such as pain, reduced functional capacity, poor sleep, fatigue, joint immobility, cognitive dysfunction, depression and anxiety. Efficacy for

pharmacologic treatment varies widely among chronic pain conditions often dictated by etiology or idiopathy. For example, methotrexate significantly improves pain, swelling and disease progression in RA and other systemic inflammatory rheumatic disease.(22) For idiopathic chronic pain and FM, pharmacologic treatments often include non-steroidal anti-inflammatory drugs [NSAIDs], topical agents like capsaicin, anti-depressants (selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors [SNRIs], tricyclics) and anticonvulsants prescribed in doses known to improve pain.(23, 24) Opioids are also prescribed; however, they are generally unsatisfactory for chronic pain with little pain resolution and undesirable side effects, physiologic dependence and risk of addiction. (25) The use of certain classes of pharmacologic treatments has remained fairly constant over time; however, in 2007, the anticonvulsant, pregabalin, became the first Food and Drug Administration (FDA)-approved drug for fibromyalgia followed by the SNRIs, duloxetine (2008) and milnacipran (2009). These approvals were momentous for recognizing and legitimizing fibromyalgia. In 2010, duloxetine was also FDA-approved for use in OA and chronic LBP. Despite this evolving landscape of drugs approved for chronic pain treatment, pain relief from these agents is generally modest; discontinuation or dropout from clinical trials is high when pain relief fails to outweigh adverse effects.(24, 26)

Non-pharmacological therapies, then, are an increasingly important component for chronic pain management. Cognitive behavioral therapy is a classic example, which uses behavior modification strategies to effectively reduce pain and fatigue, and improve sleep, overall physical function and coping. (27-29) Therapies once considered “alternative” such as acupuncture, mindfulness meditation, yoga and relaxation have become accepted forms of symptom management with clinical trials demonstrating efficacy for pain and physical function. (28, 30)

Physical activity is a well-documented, viable therapeutic modality for chronic pain conditions with beneficial effects on pain, sleep, cognitive function and physical function. (27, 30-32) Increasing evidence defines physical activity as beneficial for many chronic illnesses including cardiovascular disease, type 2 diabetes, obesity, and cancer.(16, 33) Physical activity tends to reduce the economic impact of chronic illness through improvements in overall well being, independence, and reduced healthcare seeking and workplace absenteeism.(34-36) Overall health benefits are undeniable, regardless of whether physical activity is accomplished via lower intensity (i.e., lower energy expenditure) exercise or activities of daily living, movement therapies (Tai Chi, Qigong, yoga), or higher intensity exercise associated with cardiovascular fitness gains. No single modality provides overwhelming symptom relief for chronic pain patients; rather, multimodal treatment regimens including pharmacological and nonpharmacological management strategies appear to be most effective.

Physical activity as treatment

Historical evidence for physical activity varies with the quality of randomized controlled trials (RCTs); however, the bottom line has consistently supported physical activity as a beneficial modality for chronic pain, physical function, sleep, cognitive function and overall health and disease risk modification.(37-46) Further, physical activity positively influences

quality of life, activities of daily living, emotional affect, overall physical function and independence. At the same time, physical activity reduces disability and risk of developing comorbid illnesses including hypertension, cardiovascular disease, type 2 diabetes, osteoporosis and obesity.(15, 16) With moderate to vigorous intensity, physical activity is effective – arguably, required - for weight management,(15) which in turn, effectively minimizes excessive joint loading and joint pain.(47)

Several studies have explored the economic impact of physical activity on pain and arthritis. Supervised and community-based exercise programs requiring facilities, equipment and instructors can be costly and inaccessible logistically or financially for some patients, failing to provide outcomes substantially better than usual care for the costs incurred.(48-50) Alternatively, self-directed physical activity can be inexpensive, requiring minimal resources such as walking around one's neighborhood and home-based programs. The CDC aims to make community-based exercise more feasible, less costly, and more attainable with guidelines that promote implementation and user-friendly self-management education for clinicians and patients. (40, 51)

Meeting the 2008 Physical Activity Guidelines for Americans recommendation of 150 minutes of moderate-equivalent physical activity per week(52) is not associated with worsening radiographic, symptomatic knee OA; however, many physical activity RCTs for other chronic pain symptoms such as FM do not meet these guidelines.(53) Patients and practitioners alike seek clear guidance for the type of physical activity that is most beneficial for chronic pain without exacerbating symptoms; exercise approaches and considerations for the management of chronic pain conditions are discussed below.

Major Categories of Physical Activity

RCTs have compared a breadth of activity types and environments, including aquatic vs. land-based exercise, aerobic exercise, resistance training, and movement therapies.

Aerobic exercise has long been studied as a treatment for chronic pain. Aerobic exercise includes both land-based exercise, such as walking and stationary cycling, and aquatic exercise.(16, 28, 37, 56-58) Recent studies have defined the benefits achieved according to intensity of exercise. For purposes of chronic musculoskeletal pain, intensity refers to the amount of energy expended and does not imply joint loading or impact. Quite uniformly, low to moderate intensity exercise defined as 50-60% of maximum heart rate (maxHR) tends to improve chronic pain symptoms. Moderate to high-intensity activity defined as 60-80% of maxHR, a level of intensity required to achieve cardiovascular fitness gains in the general population, has been shown to improve fitness in those patients with chronic pain who can tolerate this level of intensity. (15, 53, 59)

Strength training, defined as contracting muscles against resistance, can be accomplished using free weights, resistance machines, elastic bands, and resistance against water or one's own body weight. Strength training for FM and chronic pain is well-supported. (28, 37, 45, 60-62) Recent studies have demonstrated more robustly that strength training is both safe and effective for a variety of chronic pain conditions.(61, 62) Land-based training appears to

yield greater strength gains than aquatic resistance training.(56) Further, strength training may also improve quality of life and emotional affect in this population.(63)

Flexibility training includes exercises to improve joint range of motion and reduce muscle stiffness. Flexibility training, alone, for treatment of chronic pain was modestly beneficial for pain with a greater impact on emotional affect.(60) Similar findings exist for studies in which flexibility is part of a larger exercise program that includes aerobic or strength training. In this multimodal context, flexibility training is efficacious for anxiety, depression and health-related quality of life. (43, 60)

Interest in the effects of movement therapies such as yoga, Tai Chi, and Qigong has gained momentum for chronic pain. Generally, movement therapies are performed at lower intensity and are safe and well tolerated in this population.(33, 39, 44, 64) In addition to pain and physical function, movement therapies improve balance, mobility, joint flexibility, depression and anxiety.(39, 44, 65)

Outcomes of physical activity

Pain

For most chronic pain patients, the goal of participating in physical activity is to reduce pain. Recent studies have shown that multimodal exercise programs that include a range of activity (aerobic, resistance, and flexibility exercises) are effective at significantly reducing pain in OA, FM, CLBP and RA.(38, 66, 67) In FM patients, low-moderate intensity warm-water pool exercise performed twice per week had an immediate positive effect on pain that was sustained during the 12-week program.(68) Similarly, 12 weeks of Tai Chi performed twice weekly reduced FM pain.(39, 44) Strength training twice weekly resulted in significant improvements in pain in FM patients.(60) Eight weeks of yoga, including weekly 2-hr supervised sessions plus home practice, improved pain in 22 FM patients.(65) While improvements in pain can be immediate, benefits are still notable after long-term follow up from 24 weeks(44) to 30 weeks.(43) When performed regularly, aerobic exercise may be as effective as NSAIDs for reducing pain.(40, 69) Combining physical activity with other non-pharmacologic therapies such as cognitive behavioral therapy and self-management education for coping, socialization and adaptation may be an effective clinical strategy for pain reduction.(67, 70)

Physical function

For patients with chronic pain, improving physical function is nearly as important as improving pain. Physical function in FM has been found to be worse than that after congestive heart failure.(71) Similar to pain, a multimodal physical activity program including aerobic, strengthening and flexibility exercises will improve physical function significantly.(16, 43, 45, 67, 72-74) Movement therapies such as Tai Chi and yoga improve strength, balance and mobility as well as attenuate anxiety and depression, which in turn, yield improvements in physical function for patients with FM, OA and RA.(44, 65) Moderate- to high-intensity resistance training improve physical function with little risk of exacerbating pain or other adverse effects provided that patients follow a plan of regular activity with slow progression.(37, 41, 60) Kalesh et al.(41) allowed participants to self-

select activities meeting a MET-level for moderate to vigorous activity, and physical function improved significantly.

Sleep and fatigue

Sleep disturbance and fatigue are common symptoms for individuals with chronic pain conditions. FM patients frequently report non-restorative sleep as the fourth most common complaint behind pain, fatigue and health-related quality of life.(75) Patients specifically identify poor sleep quality and quantity (difficulty falling asleep, getting comfortable, and staying asleep); restlessness; not feeling rested upon awakening; and difficulty starting the day.(75, 76) Poor sleep exacerbates the pain, stiffness, fatigue, and attention deficits that FM patients experience.(76) Interestingly, disruptions in both sleep and exercise can also have deleterious effects on pain and mood in healthy individuals, suggesting the importance of maintaining regular habits.(77) Twelve weeks of twice weekly Tai Chi significantly improved sleep in FM patients.(39) A meta-analysis of RCTs for movement therapies noted significant improvements in sleep in 372 FM subjects.(30) While evidence shows that engaging in physical activity improves sleep, the effect is reciprocal. In the absence of an intervention, 119 chronic pain patients naturally increased their physical activity on days that followed a night of higher quality sleep. (32) These findings emphasize the importance of improving or maintaining good sleep both for pain and for physical activity.

Depression, anxiety and mood

Depression and anxiety are common among chronic pain patients with 90% of FM patients reporting depressive symptoms over their lifetime.(78-80) Further, 86% of FM patients have been diagnosed with major depressive disorder during their lifetime.(80) Poor muscle strength, a sign of inactivity, is associated with depression, anxiety and reduced health-related quality of life.(63) Depression can challenge adherence to an exercise program especially when social or psychological support is lacking.(81) Physical activity is commonly accepted to elevate mood in the general population, and the effect extends to chronic pain patients. In a recent study of 158 FM patients, those who chose active pain management strategies also had significantly less depression than patients who did not engage in these strategies.(82) The elevated mood derived from physical activity tends to be well maintained with continued exercise and persists for up to six months of detraining.(43, 57) A wide variety of activities appear to improve depression, including aerobic exercise, (41, 81) muscle strengthening,(60) and movement therapies.(30, 44, 64, 65) Moving more may be sufficient to tip the scales toward a positive mood.

Inflammation and related outcomes

Individuals with chronic pain conditions may exhibit systemic inflammation as a result of their condition or due to comorbid diseases. Physical activity is known to mitigate cellular inflammation.(83, 84) A recent study in 2330 adults demonstrated that frequency of physical activity had a greater effect on systemic inflammation than volume of activity.(85) Specifically, total weekly accumulation of physical activity was a stronger predictor of lower C-reactive protein (CRP) levels than the number of days per week of 30min/day of physical activity. Following 4 months of twice weekly aquatic exercise, inflammatory profiles improved in FM patients as interleukin (IL)-6 increased while spontaneous release

of tumor necrosis factor alpha (TNF α) decreased.(74) By the end of 8 months, spontaneous production of pro- and anti-inflammatory cytokines decreased, production of TNF α and IL-10 diminished, and circulating CRP decreased. These results support the importance of consistency of physical activity throughout the week. Among patients with peripheral neuropathy, aerobic exercise and movement therapy (e.g., Tai Chi) improved nerve function and reduced pain and sensory dysfunction.(33, 86) Given the cardiovascular disease risk in RA, improved microvascular and macrovascular function with aerobic exercise in RA patients is valuable.(87)

Exercise considerations for chronic pain conditions

In a review of 46 studies, Jones et al.(53) noted that the physical activity programs described in many chronic pain studies did not meet CDC and American College of Sports Medicine (ACSM) guidelines. Kelly et al.(46) deferred to the ACSM guidelines for older adults due to the lack of other specific guidance for chronic pain patients. A 2010 review of 35 RCTs for aerobic exercise in 2,494 FM patients yielded a recommendation for both water- and land-based activity of low to moderate intensity, performed 2-3 times per week for at least 4 weeks.(57) Many recent studies demonstrate significant improvements in pain, depression, anxiety and quality of life in chronic pain patients with low to moderate intensity exercise performed only 2-3 times per week.(41, 60, 64, 66, 69, 72, 88) However, acute strenuous bouts of aerobic and isometric exercise induce hyperalgesic effects in FM patients.(54, 55) Chronic pain patients may be more successful when they can self-select a lower exercise intensity than standard guidance suggests.(53) Chronic pain patients vary greatly in their abilities and limitations, goals and lifestyle, and appear to have greater success from guidance that is tailored to their specific needs, hindering the development of strict guidelines specific to chronic pain; nevertheless, daily activity should be encouraged, even if the intensity is low and duration is short.

Nonpharmacological treatments require patients to participate actively for an extended period of time, often a lifetime. Such adherence may require significant behavior change and can be difficult to accomplish; however, these activities are often the most empowering and yield the largest improvements in symptoms and overall quality of life.(58) Programs that begin with a low level of intensity and progress steadily tend not to exacerbate pain and stiffness and yield greater adherence, less attrition and overall improvement in quality of life and ability to complete activities of daily living.(53, 69) Evidence in LBP and knee OA suggests that treatment effects may increase with the number of exercise sessions performed and, in general, pain does not increase along with an increase in volume of activity.(38, 41) Thus, treatment design and approach are critical.

Exercise approaches for the management of chronic pain conditions

As mentioned above, a wide range of exercises are supported for reducing pain and improving physical function in patients with chronic pain conditions. For FM, RA, and OA pain management, effects from physical activity have been found to be largely comparable to those for simple analgesics and NSAIDs.(69, 88-90) Not only is exercise beneficial for

mild to moderate pain conditions, but those with severe pain may exhibit improved function and reduced pain with physical activity.(33, 91)

Physical activity should be recommended to all patients with chronic pain conditions. Avoidance of exercise during acute symptom flares may be tempting, but sedentary behavior may not reduce symptoms and may promote loss of strength, reduced range of motion, and physical limitations. (18-21, 38) Small amounts of activity confer reasonable to large benefits, especially in patients who transition from sedentary to active. Once active, continued improvements may plateau over time but maintenance of reduced pain-related symptoms and overall fitness is manageable with regular activity. Physical activity is generally safe with few adverse events reported in RCTs for chronic pain. Side effects are typically temporary and often avoidable with patient education and safe progression.

Optimal methods for supporting physical activity for patients with chronic pain conditions are not well-established, but the general consensus across medical and research communities is that movement, no matter how minimal in duration or intensity, is desirable. For patients with knee OA, some evidence supports exercise programs of 12+ visits with direct supervision. (89, 90) This level of supervision is often not available or feasible, plus some individuals prefer physical activities that can be done independently. When encouraging physical activity, providers should consider the patient's exercise interests and activity modifications. Frequency of physical activity is critical, especially for reducing overall sedentary behavior. To promote ongoing activity and a lifestyle change, patients may be more likely to pursue activities that they enjoyed in the past or new and exciting activities. With appropriate modifications, most forms of physical activity are acceptable for people with chronic pain conditions. Important considerations for tailoring a physical activity or exercise program include: 1) safety precautions to reduce risk of falls and injuries, 2) proper posture and body mechanics to reduce abnormal or excessive joint loading, 3) performance of exercise within a range of motion that does not increase pain or increase risk of joint instability or loss of balance, and 4) adherence to a “start low, go slow” plan of progression to minimize hyperalgesic effects of “over-doing it.”

Overcoming barriers and reaching success

Psychosocial issues compound patients' efforts to adopt and maintain physical activity and to achieve successful outcomes. Fear-avoidance beliefs and behaviors are known barriers to increasing activity and can predict functional capacity and disability.(92, 93) Fear of falling contributes to sedentary behavior in patients with chronic musculoskeletal pain,(94) and fear of increased pain and post-exertional malaise are significant barriers to activity among patients with FM and chronic fatigue syndrome.(95-97)

Chronic pain patients vary in self-efficacy (i.e., belief in own ability to complete tasks or reach a goal). Inadequate self-efficacy for exercise may be a considerable barrier to increasing physical activity and reducing sedentary time. In 41 patients with RA, physical activity time was not related to pain but was associated with self-efficacy for physical activity. (98) An RCT of 202 middle-aged to older sedentary adults supports monitoring of

adherence and individual tailoring of exercise programs to promote exercise self-efficacy and exercise maintenance. (99)

Individually or in combination, pain, poor sleep, depression, anxiety, fear-avoidance beliefs, poor self-efficacy for activity can negatively impact motivation. Tailoring exercise may significantly contribute to patients' motivation, self-efficacy and adherence. Celebrating patients' "success", symptom reduction, modeling from other successful patients, education on motivation techniques, and verbal encouragement through motivational interviewing are strategies that improve self-efficacy and motivation for exercise. (28)

Summary

Research exploring the impact of physical activity on chronic pain has grown significantly over the last 25 years with several recurring findings and limitations. Despite studies of varying quality, results consistently support the benefits of physical activity for treatment of chronic pain, both alone and as part of a multimodal program with pharmacotherapy and cognitive behavioral therapy. The impact of exercise on illness progression is largely unknown. Unfortunately, chronic pain-specific recommendations to guide patients and providers on measurable parameters (time, intensity, and frequency) are lacking. While guidelines offer a dual perception of legitimacy and comfort in prescribing exercise, chronic pain patients tend to be most successful when physical activity is tailored to their needs and limitations. Any amount or type of movement is advantageous over sedentary behavior, allowing for significant latitude in prescribing activity. Engaging chronic pain patients in a lifetime of physical activity to improve their pain, physical function, and quality of life is a classic illustration of the art and science of medicine.

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Practice points

- Understand predominant symptoms of various chronic pain conditions to discern similarities, differences and comorbidities.
- Review existing physical activity guidelines for healthy adults and older adults to improve understanding of general parameters for prescribing physical activity.
- Tailor physical activity to the specific needs and limitations of each chronic pain patient with consideration given to patients' physical abilities, emotional needs and barriers, personal interests, available resources and socioeconomic status.
- Multimodal therapy, including physical activity, pharmacotherapy, cognitive behavioral therapy, and self-management education, may be most effective for chronic pain management.

Research agenda

- Exploring the effect of exercise on disease pathogenesis for chronic pain.
- Studying the impact of physical activity on workplace absenteeism and productivity among chronic pain patients.
- Testing interventions to promote self-efficacy for exercise.