Chapter 14

Exercise for chronic pain

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The neurobiology of pain

Introduction

Pain is integral to the human experience. It is ubiquitous and omnipresent, but it has been perhaps one of the most misunderstood and misrepresented elements of the human condition. Our pervasive misunderstanding of pain was built on the Cartesian theory of pain that emerged with Rene Descartes' 1664 "Treatise of Man" (Fig. 1) [1]. This inextricably linked pain to tissue damage in our collective consciousness and it has taken us more than three centuries to begin to emerge from its' shadows and to understand our "Catastrophic misinterpretation" [2–5].

The equation of hurt and harm, or pain and damage, coupled with continuous communal reinforcement has led us to an almost society-wide "fear-avoidance" behavioral pattern. A pattern that is now postulated to underlie the chronification and persistence of pain, by driving a "vicious cycle of avoidance," disuse, deconditioning, and decreased tolerance for exercise and physical activity that eventually induces activity-dependent hyperalgesia (Fig. 2) [6–8]. No surprise then that we find ourselves seemingly on the runaway train of a chronic pain pandemic.

It's estimated that around one in five of us will suffer from persistent pain, a rate that is mirrored fairly uniformly across the globe [8–12], and pain, affecting more of us than diabetes, heart disease, and cancer combined, is the single most common reason for medical consultations. With an estimated 100 million Americans and as many as 1 billion sufferers worldwide, it is a problem that pervades all of society. It seemingly knows no bounds, but it does not affect us all equally. For example, Table 1 presents a snapshot of the incidence of chronic pain in Australia.

While this snapshot is of chronic pain in Australia it is important to note that the picture painted by this data is fairly consistent the world over, though a trend toward increased prevalence in developing countries is clearly apparent. The bottom line is that chronic pain can affect anyone, but an assortment of modifiable and non-modifiable factors contributes to increased risk [8]. Pain persistence is very strongly associated with advancing age and lower socio-economic status where poorer education, poorer health literacy, financial pressures, and a lack of early access to appropriate care, all play a role. These factors intersect sharply with sex and gender, and more sharply still with culturally and linguistically diverse populations, where care choice is often further limited by cultural and language barriers (Table 2) [8,10,11].

The impact of chronic pain

The impact of chronic pain is profound, on the individual, their social network, and the broader community. And if we are honest as practitioners, many of us would probably say that it can have a profound effect on us too. In interrogating these impacts, it is imperative that we understand and acknowledge that there are two key perspectives to be considered, the individual and the cohort. The individual stories are of the human cost to lives irrevocably changed, curtailed by distress and disability. The broader cohort and economic data are what so frequently informs policy, care allocation, and funding. These two perspectives, with much overlap, and seemingly working with the same outcomes in mind, are often juxtaposed and conflicted; frequently unable to find a middle ground. The impacts on the individual are broad-ranging and well documented.

Mood disturbance is very common in persistent pain sufferers [5,8–10,12–14]. Almost 45% experience depression and/or anxiety, which is about four times the rates seen in those without chronic pain [8,9,14]. Other psychopathology is more prevalent also. Persistent pain patients are more likely to suffer post-traumatic stress disorder (PTSD), develop substance abuse issues, experience suicidal ideation, and indeed attempt suicide [5,8,9,13,14]. In Australia alone, we lose

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FIG. 1 The Cartesian theory of pain conceived of a single "wire" carrying signals from the periphery to the brain. The fundamental premise here was that if there were no fire, there could be no pain [1].

around 1000 people to prescription opioid misuse each year [9]. The WHO puts the global number at around 150,000 each year.

Sleep disorders are almost synonymous with chronic pain, affecting between 5 and 9 in every 10 patients with persisting pain [14–19]. The degree of sleep disturbance appears to correlate strongly with pain intensity and the relationship is clearly bidirectional, meaning the two problems are prone to perpetuating one another [14,15]. Managing pain early is key to minimizing sleep disturbance and managing sleep disturbance is pivotal in managing pain [5,8,14,15,17].

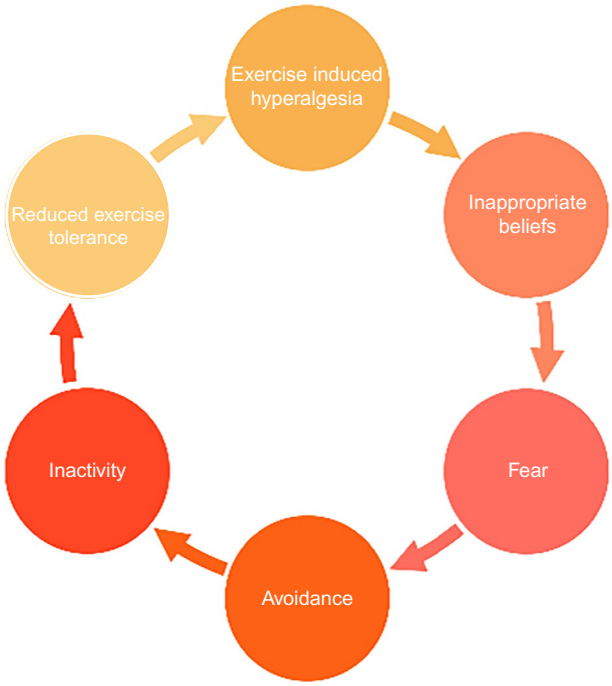


FIG. 2 Our catastrophic misunderstanding of pain and its flow-on effects. *Adapted from Meeus et al. [6].*

TABLE 1 A snapshot of chronic pain in Australia.

In 2018 3.24 million Australians lived with persistent pain
Of these 54% were women; 46% were men
Almost 70% were working age, but only ~25% maintained employment
Prevalence increased with age (1/3 of Australians aged 65+ lived with chronic pain)
Young adults were less commonly but typically more profoundly affected
25% of kids experienced chronic pain (this was moderate to severe and debilitating for ~5%)
Chronic pain is more prevalent in rural communities
Back pain is 23%–30% more likely in people living outside of major cities
Multi-disciplinary pain care is less prevalent in rural, regional, and remote areas

Adapted from Economics [9].

TABLE 2 Risk factors for chronic pain [10].

Non-modifiable	Advancing age Female sex Cultural background Socio-economic background History of trauma, injury, or interpersonal violence Heritable factors (including genetic)
Modifiable	Other pain (acute or chronic) Mental health Obesity and other co-morbidities Smoking and alcohol consumption Physical activity/exercise Sleep Nutrition Employment status and occupational factors

Cognitive decline and executive function deficits are also prevalent in chronic pain patients [8,14–16,19,20], with memory and attention deficits being estimated to affect as much as 65% of the chronic pain population [14,19]. This can be a major obstacle in conducting daily activities and is most certainly an obstacle to effective recovery.

Implications for cardiovascular health are well established. Chronic pain has been repeatedly determined as a stand-alone predictor of hypertension and a risk factor for other cardiovascular diseases and events, independent of age, sex, race, and familial history [14,21–23]. Changes to cardiovascular health and risk are thought to center around baroreflex changes gearing them toward antinociception or pain suppression. A normal adaptive change in acute pain, that when prolonged leads to baroreceptor hyposensitivity and increased risk for hypertension (HT), and increased morbidity in those with existing coronary health disease (CAD) [14,22]. Interestingly though, a patients' perceived disability has been shown to have an even greater impact on cardiovascular risk than the severity of the pain itself [14]. Perceived disability and physical activity avoidance go hand in hand, so the compounding of cardiovascular (CV) risk here is probably more obvious than may first be apparent.

Overall quality of life is significantly impacted for chronic pain patients [8,9,14,16,24–26]. Relationship decline, sexual dysfunction, reduced social interaction, increased distress, and perceived disability all play a role [14,16,20,24]. The severity of these effects largely appears to increase with pain intensity [14,20]. Where pain and disability are such that they interfere with employment continuity, further distress and financial stress typically ensue, with negative effects on relationships and social participation further compounded [14,24]. Chronic pain is the single most common reason

Australians cite for dropping out of the workforce and with almost 70% of our persistent pain population being working age and only around 25% being able to maintain employment, this is a sizable problem for not only the individual but the wider community also [9].

Physical activity is significantly reduced in those with chronic pain [5–9,11,16,20,24,25], and much like sleep disturbance, this is an element of the condition that can perpetuate pain [5–8] and indeed, requires its own management strategies and interventions [6,11,14]. Concomitant pain and physical inactivity work to not only perpetuate one another but compound the other deleterious health and quality of life impacts of chronic pain also [11,14].

The economic impact

In 2018 alone, the total financial cost of chronic pain in Australia was estimated at $73.2 billion. This included $12.2 billion in health system costs, $48.3 billion in lost productivity, and $12.7 billion in other financial costs and losses, such as informal care, and aids and modifications [9]. In America, lost productivity from pain conditions is estimated to cost $61 billion annually, in Sweden it is just shy of 80 billion SEK [27]. Quality-of-life (QOL) losses however are not just personal and come at a cost to the broader community also [9,24]. These losses can be translated into economic terms using the World Health Organization (WHO) Burden of disease methodology to account for the cost of years of life lost due to premature death (YLLs) and years of healthy life lost due to disability (YLDs). This system puts the Australian 2018 cost of quality-of-life losses at $66.1 billion. The combined financial costs and QOL costs take the Australian 2018 total cost of chronic pain to $139.3 billion. If the status quo is maintained in terms of treatments, prevalence rates, and real costs per person, this figure is expected to jump from $139.3 to $215.6 billion by 2050 [9]. While this data is again largely Australian, the trends are global. Something needs to change.

Defining pain

We have struggled to define and describe the pain and, in recent times have come to acknowledge a dearth of language to adequately capture and characterize the complexity of the pain experience. This is likely a reflection of the multifaceted nature of pain and its wide-ranging effects that commonly impact our sensory, emotional, and cognitive experiences.

From the International Association for the Study of Pain (IASP):

Pain is "An unpleasant sensory and emotional experience associated with, or resembling that associated with actual or potential tissue damage," and is expanded upon by the addition of six key notes and the etymology of the word pain for further valuable context.

- Pain is always a personal experience that is influenced to varying degrees by biological, psychological, and social factors.
- Pain and nociception are different phenomena. Pain cannot be inferred solely from activity in sensory neurons.
- Through their life experiences, individuals learn the concept of pain.
- A person's report of an experience as pain should be respected.
- Although pain usually serves an adaptive role, it may have adverse effects on function and social and psychological well-being.
- Verbal description is only one of several behaviors to express pain; inability to communicate does not negate the possibility that a human or a nonhuman animal experiences pain [28].

Chronic or persistent pain is simply pain that "persists beyond normal tissue healing time, which is assumed to be three months" [29]. This definition, scant as it is, has stood for decades unaltered. Recently however the IASP and the WHO have expanded the definition and classification of chronic pain to distinguish between primary and secondary chronic pain syndromes [28]. Critically, this update acknowledges that although chronic pain can be a symptom of another disease, it frequently occurs without clear cause and can be considered a neurological disease characterized by changes primarily to the central nervous system [14,28]. This sort of primary chronic pain syndrome accounts for 17% of chronic pain in Australia [9] and making this acknowledgment is a critical steppingstone in the development of targeted research and eventually, better treatment protocols.

Pathophysiology

Regardless of the initiating illness or injury, or indeed whether there was one at all—it is to a seemingly significant extent that the inherent plasticity and adaptive capabilities of the nervous system, encode and drive the sensitization that underpins persisting pain [5,6,8,30–32]. Understanding this unifying pathophysiology of pain persistence adds leverage to managing

those with secondary pain syndromes, and crucially, adds therapeutic avenues for those with primary pain syndromes who are otherwise often left on a fruitless and often maddening search for something to treat. The pathophysiology that unifies almost all persisting pain is extremely complex, indeed entire textbooks have been devoted solely to the transition from acute to chronic pain. While pain physiology is typically considered the domain of neuroscience, the pathophysiology of chronic pain cuts across a number of complex systems and is better thought of as an integrated function of the neuroimmune-endocrine axis. There are however pragmatic ways in which we can simplify this complexity for clinical translation. The application of a top-down, bottom-up information processing approach can be readily applied with good clinical utility [33].

Bottom-up pain processing

Nociception is the fundamental bottom-up pain process, but nociception is not pain. While nociception is usually described as leading to pain perception, it is insufficient alone to explain pain [8,34] and, pain without nociception and nociception without pain are both well-substantiated phenomena [5,8,28,31,32]. Nociception is in essence a warning shot, signaling the detection of a potential threat. It is comprised of four key processes:

- Transduction
- Transmission
- Perception
- Modulation (takes place at all levels of the nervous system and influences the first three processes both directly and indirectly)

These processes are inherently adaptive and plastic to allow for amplification and attenuation of nociceptive signaling and pain perception, to balance the allocation of neurophysiological resources between the task at hand and the need for survival [8,30,34]. While we tend to talk about these modulation processes in the context of pain, illness, injury, and indeed recovery—it is important to note that sensitivity to all stimuli is continually modulated moment-to-moment by a combination of intra and exteroceptive inputs.

Key concepts in bottom-up pain processing

Bottom-up processing of nociceptive inputs is largely a function of the peripheral nervous system and spinal cord. Though both amplification and attenuation mechanisms exist at all levels of the nervous system, bottom-up processing is heavily geared toward amplification to ensure nociceptive salience and appropriate behavioral responses to threats [32,34]. To this end, there are a number of mechanisms built in that allow us to respond more readily and more intensely to potentially threatening stimuli [30–32,34,35].

Peripheral sensitization mechanisms

The first component in our protective pathways are the primary afferent nociceptors, these are our ‘ground troops’ in threat surveillance and detection. These nociceptors are a molecularly diverse collection of free nerve endings that respond to a broad range of stimuli, with varying degrees of sensitivity [8,13,32,34]. Each nociceptor will respond preferentially to a particular stimulus type (allowing for specificity) but the diversity of receptors within each nerve ending will also allow for generalized recruitment and contribution toward a stronger response to a non-preferred stimulus when potentially advantageous [34]. This essentially amplifies our ability to respond to intense, potentially threatening stimuli. The diversity of these nociceptive neurons allows for several modes of classification, the most useful (clinically speaking) include:

- Fiber diameter (giving fast/slow or first/second pain phenomenon).
- Transduction threshold (giving varying degrees of mechanical sensitivity and allowing for heightened mechanical sensitivity in the presence of inflammatory mediators).
- Stimulus they respond preferentially to.
- Peptidergic capacity.

These nociceptors begin to detect, transduce, and transmit threat signals in response to tissue stressors, well before tissue tolerance thresholds are reached. Meaning they build into our threat response system, a protective buffer that allows us to be predictive and protective [5,8,13,30,32,34]. Because of this, neither nociceptive signaling nor indeed pain perception are predicated on tissue damage. A clear and simple example of this can be found in our responses to potentially threatening thermal stimuli (Fig. 3).

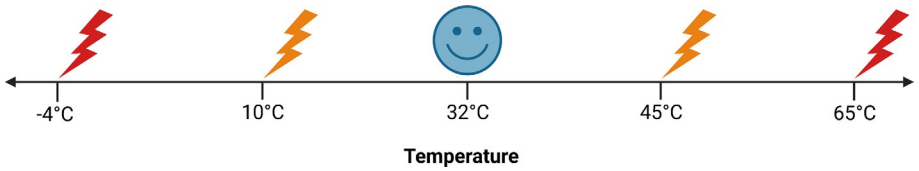


FIG. 3 The protective buffer. A simple diagram for explaining the protective buffer to patients, demonstrating clearly how nociceptive signaling and pain perception are not reliant on tissue damage.

Cutaneous heat pain thresholds are consistently lower in women than men and can vary with ambient temperature and rate of temperature change [35,36], etc., but on average it is generally accepted that humans will begin to perceive pain at around 44 or 45 °C [35]. Physiological signs of thermal injury at these temperatures, however, would take 3–6 h to develop. Instantaneous or near-instantaneous cutaneous tissue injury does not develop until temperatures are >60 °C. This clearly demonstrates a 15 °C or ~30% protective buffer. A similar buffer is found at the other end of the spectrum with cold pain and injury thresholds. Cold pain is more variable than heat pain but is frequently perceived from around 6–10 °C, while the injury is not typically noted until <0 °C [35].

As nociceptor function is continually adjusted, these protective buffers are subject to continued modulation and as noted, we have numerous mechanisms for enhancing sensitivity and enhancing this buffer, particularly in the presence of inflammatory mediators. While designed to ensure protection when under a perceived threat, in the case of spontaneous chronic pain, sensitivity can blow out to such an extent that these warning signals are being fired under completely normal, innocuous stimulus conditions [8,13,30,37,38] (Fig. 5).

The peptidergic capacity of a neuron refers to its ability to generate and release its own inflammatory peptides via an axonal reflex, in response to activation. This is a key element of the initiation and maintenance of peripheral sensitization (Fig. 4) [8,13,30,37].

About 40% of our dorsal root ganglion cells are peptidergic in nature, producing neuropeptides such as substance P and Calcitonin gene-related peptide (CGRP), to initiate neurogenic inflammation [8,34]. This inflammatory response comprises vasodilation, plasma extravasation, smooth muscle contraction, and mast cell degranulation. This is typically a focal response, localized to areas of actual or potential tissue injury, that can then be augmented by central processes, in response to tissue stimulation or top-down facilitation [13,34,38].

In essence, these free nerve endings both act in response to and produce inflammation as a means of priming and enhancing the immune response to tissue injury. This drives a positive feedback loop that escalates both sensitivity and tissue repair processes [8,34,38]. G protein-coupled chemoreceptors respond to inflammatory chemicals such as histamine

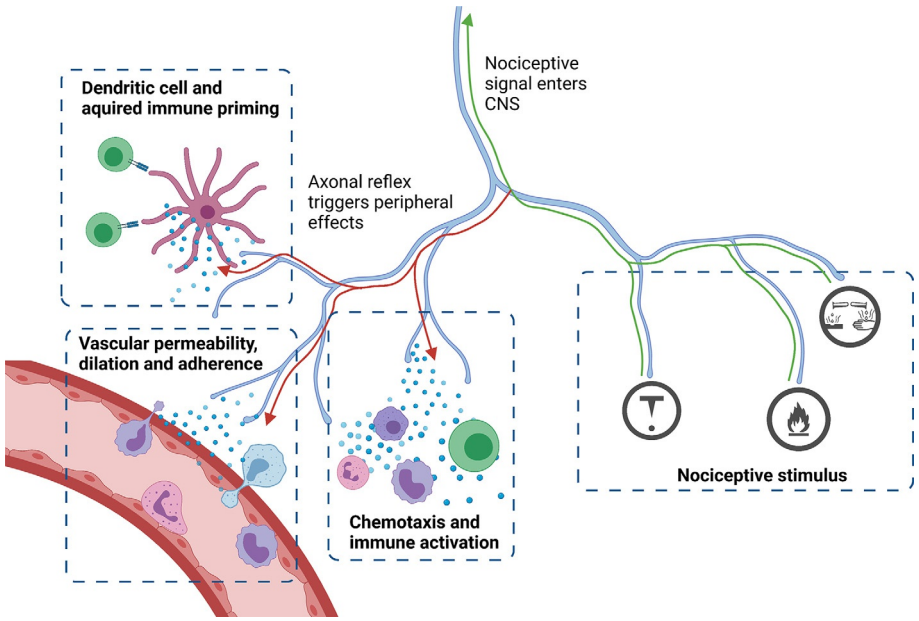


FIG. 4 The axon reflex.

prostaglandins, serotonin, bradykinins, interleukins, nerve growth factor as well as intra cellular substances such as ATP, glutamate, and adenosine [34,38]. A second messenger cascade has two-fold effects: sensitizing associated membrane channels and up-regulating receptor and neurotransmitter production signals at the neuron's nucleus [13,34,38]. The net effect of these changes can be summarized as follows:

- Existing membrane receptors become more sensitive, they open in response to lesser stimuli and stay open for longer.
- The neurons will exhibit higher frequency firing as a result.
- The neuron may also develop more receptors to the same stimulus to further boost neuronal firing and facilitate the release of enhanced neurotransmitter stores.

Clinically these changes manifest as hyperalgesia and allodynia [34,39,40]. They are a normal part of the pathophysiology of pain and tissue injury and should be thought of as a short-term enhancement of immune and recuperative behaviors. They should reverse and revert to the patient's normal baseline as the tissues heal or even earlier if the threat is assessed as being insignificant. Many of these changes can be described as semi-permanent in nature and it is important to acknowledge that when inflammatory processes persist, sensitization is also likely to persist, increasing the risk of central sensitization disorders [33,40–42]. It is also important to acknowledge however that many of these changes are inherently reversible and when pain conditions are managed well at the onset of episodes, progression to centrally sensitized states would appear to be much less likely [33,42].

Spinal sensitization mechanisms

The axonal reflex that dumps inflammatory cytokines into peripheral tissues has an orthodromic counterpart. This means that the cytokine dumping that initiates and maintains peripheral sensitization is mirrored by cytokine dumping at the dorsal horn of the spinal cord and unsurprisingly, this initiates and contributes to the maintenance of a state of spinal sensitization. Spinal sensitization has a number of unique features that are reflective of the neuroanatomical organization of the dorsal horn and cord, where primary to secondary synapses reside. The general theme of cord organization is convergence; convergence of many primary afferents onto a single secondary, the convergence of noxious and innocuous information processing, the convergence of interoception and exteroception, and importantly, parallel organization of autonomic and somatic functions (sympathetic). Finally, there is the convergence of multiple dorsal roots into the cord as stacked segments to consider [8,30,33,37,40,41].

The first and most clinically apparent difference resulting from all this convergence is that it allows for sensitivity to develop across far larger body areas. This tends to present with regional pain syndromes as opposed to the local pain seen with peripheral sensitization. It also means that spinal sensitization can give rise to pain referral within and across body systems and can also give rise to sympathetically maintained pain [8,30,33,37,40,41]. This drawing in of the autonomic nervous system and its ties to the HPA axis is pivotal to our understanding of chronic pain. All in all, spinal sensitization is a more complicated pathophysiological process than peripheral sensitization, but it is also one that reinforces peripheral processes, making the amplification cycle harder to break. This comes in the form of antidromic prostaglandin dumping from second-order relays and creates a positive feedback loop across the primary to the secondary synapse, meaning that activation of the second-order nociceptive neuron reinforces sensitization of the primary [30,32,33]. Again, this is designed to ensure nociceptive salience and will be subject to top-down dampening when deemed appropriate [13,43].

Without diving too deeply into the detailed processes here, there are some key parallels to peripheral processes that are worth covering off. Much like in peripheral sensitization processes, we see some short-term changes to neuronal behavior (activity-dependent wind-up that is inherently reversible) [13,31–33,37,43] but sustained Ca^{2+} influxes, increased intracellular Ca^{2+} mobilization and subsequent alterations in gene transcription give rise to the production of modified NMDA and AMPA receptors that effectively have longer channel opening, at lower levels of stimulus and faster associated plugging of the NMDA Mg2+ receptor blockade. When combined, these changes drive a more prolonged postsynaptic hyperexcitability in secondary afferents [13,33,37,41,43].

Activation of cord sympathetics has also been implicated in the activation and sensitization of primary afferents, and the maintenance of peripheral inflammatory processes in chronic pain patients. This is just one interaction between the sympathetic nervous system and pain, there are many more at all levels of the neuraxis but this one serves to set the scene for a key deviation from normal, acute pain physiology that we see in chronic pain. In healthy individuals, this sort of activation would commonly result in antinociception via top-down inhibitory pathways (discussed in more detail later) but in chronic pain patients where these modulatory processes get somewhat distorted—we commonly see descending inhibition replaced by descending facilitation and long-lasting nociceptive sensitization to stress hormones develop. This change is thought to be key to pain taking on a life of its own that no longer seems related or proportionate to physical stressors. Afferent

hyperexcitability is also thought to be further augmented and sustained by cord glial cell activation in response to peripheral inflammatory insult and/or injury. Astrocytes and microglia are particularly involved here, orchestrating changes to neurotransmitter reuptake and extracellular ion homeostasis [13,37,44,45].

These processes are thought to be a key underpinning of the fundamentally abnormal response to sensory stimuli we see in chronic pain patients [13,40,43]. While these changes are all largely reversible it is important to acknowledge that again they are in effect, semi-permanent in nature and their self-reinforcing nature inherently reduces the plasticity of the system, particularly when sustained over longer periods. One key exception to the "sustained over long periods" notion is neuropathic pain, where dramatic structural plastic change can be noted in both neurons and glial cells, after even very brief periods. This is covered in another chapter but is an exception worthy of noting here.

Supraspinal sensitization mechanisms

These second-order nociceptive afferents are much more diverse than their primary counterparts. Somatic nociceptive relays largely arise in the dorsal horn of the cord and traverse the anterolateral system, while secondary visceral afferents largely arise in the brainstem after receiving inputs via the dorsal column medial lemniscus system [34,35,40]. Some travel ipsilaterally and some contralaterally, some encode contralateral information, and some bilateral. They terminate on tertiary neurons located in numerous parts of the brainstem and diencephalon. This diversity speaks to the diversity of function but also the imperative of survival and preservation of nociceptive salience.

In broad terms these pathways relay nociceptive information for the following purposes:

- to the thalamus and cortex for processing and perception of pain
- to the brainstem and hypothalamus for coordinating autonomic responses to pain
- to the medulla and midbrain for endogenous pain modulation
- to the limbic system for motivational-affective pain perception

Less is known about nociceptive modulation processes at the secondary to tertiary nociceptive synapses, or indeed at the third-order neurons of these pathways. But what we do know so far raises suspicions that many of the changes seen at the primary and secondary afferents to ensure nociceptive salience, may in fact be mirrored at tertiary nociceptive neurons [40]. This appears to manifest as both direct facilitation and/or disinhibition of the secondary relays [46], which are of course "top-down" processes and will be discussed further in the coming paragraphs.

Animal studies have demonstrated thalamic hyperexcitability in the presence of peripheral inflammation and injury [47] and, due to further convergence in the system, these neurons have even larger (some even have whole-body) receptive fields that may manifest clinically as chronic widespread pain (CWP) syndromes [41,48]. It is presumably also due to changes at this level that we begin to see distortions of hypothalamic and autonomic function in response to pain. These changes are characterized by sympathetic hyperarousal and to date, provide the clearest, measurable clinical indication of the acute to chronic transition.

Ostensibly, it follows that sustained changes here are a driver of the broader autonomic and endocrine dysfunction we see longer term in patients with chronic pain. This certainly appears to be the case when we look at changes to blood pressure regulation and longer term dulling of baroreceptor sensitivity [22,23]. It is probably not a far reach then to propose that these sorts of changes may underlie the myriad systemic changes and increased health risks we also see in more complex persistent pain presentations. Though largely speculative these sorts of changes are also thought to contribute to changes in the downward modulation of pain via the PAG, RVM, and amygdala. We can infer that this may manifest as impaired inhibitory modulation, the perpetuation of facilitatory modulation, altered behavior, and fear conditioning and may also be associated with anxiety states. This flow on to alterations in top-down modulation and the critical role of the amygdala will be covered in more detail in the next section.

Top-down pain processing

The top-down processing of pain-related information has two key purposes, it largely works toward the modulation of bottom-up (nociceptive) inputs and toward driving appropriate behavioral responses (both somatic and autonomic) to nociceptive stimuli. As noted previously, modulation is a constant tug of war between inhibition and facilitation to balance the allocation of resources and better the chance of survival. Top-down modulation is key to this process and is essentially tasked with determining whether nociception and pain are safe to ignore and attenuate our perception and responses to, or whether protective responses require amplification to enhance prospects for survival. This

assessment appears made largely with respect to nociceptive inputs, the context of those inputs, and the previous experience and expectations of the individual [49].

The central nucleus of the amygdala (CeA) is particularly implicated here with the recent works of Wilson et al. (2019) eloquently conceptualizing the CeA as a pain rheostat that allows us to flick between the dual and opposing functions of nociceptive amplification or attenuation according to the context of the nociceptive inputs and, experience and expectations of the individual [49]. To accomplish this the CeA appears to weigh inputs from the thalamus, somatosensory cortex, and limbic cortices with nociceptive information from the cord; discharging orders to influence pain and pain-related behaviors via feedback loops to descending modulatory systems (via the substantia nigra, locus coeruleus, and Raphe nuclei of the medulla) [46,49].

These descending pain modulatory systems arise within the brainstem to send processed pain outputs to the dorsal horn (DH), where they modulate peripheral nociceptive inputs via either direct synapses or indirectly via volume transmission [13,46]. Nociceptive inhibition or antinociception is actioned and has marked evolutionary value where pain runs counter to the aspiration of survival. Nociceptive facilitation is used to prioritize protective behaviors and to enhance sensory transmissions from areas of, or adjacent to, compromised sensory surveillance. This is a system in flux, but persistent pain drives a positive feedback loop that reduces the inherent plasticity of the system and makes the return to baseline harder and harder as time goes on. Baseline should be the normal homeostatic setpoint of antinociceptive dominance when not under threat but for individuals with chronic pain, downward facilitation and nociceptive amplification commonly persist despite the absence of illness, injury, or threat.

The PAG-RVM system

The periaqueductal gray (PAG)—rostral ventromedial medulla (RVM) system is not alone in modulating nociception from above, but it is the system we currently understand the most about. The PAG plays key roles in autonomic and motivated behavior, particularly in response to threatening stimuli. It receives input from the spinomesencephalic tract and the rostral anterior cingulate cortex, hypothalamus, and amygdala to ensure moment-to-moment influence from both bottom-up and top-down processing systems [8,13,40,46]. These inputs importantly convey mechanisms by which, thoughts, emotions, stress, fear, and illness may influence nociceptive modulation within the system. The PAG projects opioid encephalin releasing neurons to the Raphe nucleus magnus in the RVM and the RVM contains a range of neurons thought to act as the final common pathway for several top-down modulatory systems [50]. These neurons then project to the superficial (and to a lesser extent deep) DH laminae where they either inhibit or facilitate A & C fiber sensory transmissions depending upon the influence of the PAG and CeA (among other inputs) [49,50].

The bulk of descending RVM neurons appear to be GABAergic and glycinergic and these are thought to mediate general anti-nociception at the DH [50]. The system's default operational mode appears to be to suppress C fiber nociception at the superficial DH. The RVM's serotonin-releasing neurons can have either inhibitory or facilitatory effects at the DH depending upon receptor subtypes they interact with. Facilitatory roles appear particularly relevant in inflammatory and neuropathic pain states. The PAG and RVM both have reciprocal connections to noradrenergic pontine nuclei, most notably the locus coeruleus. This appears to be another key component of the downward modulatory system [46,50]. Like the RVM's serotonergic neurons, noradrenergic neurons appear to exert excitatory or inhibitory effects dependent upon receptor subtypes they interact with also.

This ability to switch between downward inhibitory and facilitatory functions appears to be pivotal in our understanding of the acute to chronic transition and it would appear that "getting stuck in facilitatory mode" is a crucial step toward severe and intractable pain. While these modulatory pathways are therapeutic targets for serotonin/noradrenalin reuptake inhibitors and opioids, their influencing inputs make a clear biological connection for educational, cognitive, and talk therapies to be harnessed for analgesic effect. Their connections to cardiorespiratory centers in the brainstem that initiate and enhance antinociceptive effects in normal, healthy individuals also open avenues for exercise therapies to be used as targeted retraining in some. And indeed, there is evidence to suggest that reversal of baroreceptor desensitization with regular huff and puff exercise is coupled to improved descending inhibitory function and reductions in pain for some patients.

Diffuse noxious inhibitory control (DNIC)

DNIC refers to the curious phenomenon of pain in one part of the body inhibiting the perception of pain elsewhere [51], likely a mechanism developed for managing attentional load when under threat. The caudal medullary subnucleus reticularis dorsalis (SRD) appears to operate a parallel system, completely independent of the PAG-RVM system, to exert antinociceptive effects on the deeper wide dynamic range (WDR) neurons of the DH [51]. Under the influence of key cortical

areas, the SRD conveys projections to the DH and CN V nociceptive neurons via the dorsal column medial lemniscus (DCML) system [46,50,51]. DNIC appears to be under the sway of an equally diverse range of cortical inputs that further support therapeutic pathways for non-pharmacological interventions, these include:

- Prefrontal cortex (attentional control for sensory processing, behavioral planning)
- Anterior cingulate cortex (cognition, evaluation of pain and its impact, pain avoidance)
- Midcingulate cortex (fear and unpleasantness of pain, motor responses to threat)
- Insular cortex (pain behaviors in response to PFC, ACC, amygdala, and hippocampal inputs)
- Amygdala (learned fear, fear-avoidance, anxiety, modulatory control)
- Hypothalamus (stress responses, autonomic and endocrine control)

These top-down processes are more complex again and are typically more challenging for patients to understand, but there is great value in prioritizing helping our patients to understand and indeed exploit these therapeutic avenues. There is good evidence now to suggest that impairment of endogenous inhibition and/or augmentation of endogenous facilitation are associated with chronic pain states [13,40,46,50] (particularly those where pain is spontaneous or has a life of its own because transmission is no longer predicated on presynaptic or primary afferent activity) and while these are often late changes in nociceptive pain conditions, they can occur much faster in neuropathic pain conditions and in those genetically and historically predisposed.

Selecting medicines and other therapeutic interventions that reflect the predominant pain type and sensitization mechanisms will tend to provide the patient with the best outcomes. Taking a multifaceted approach that utilizes a combination of interventions to target these mechanisms, will allow for compounding of effects and a better outcome overall. When pain is viewed as a biopsychosocial phenomenon and its potential to be or become a pathology in its own right is acknowledged, the value of exercise as both a treatment goal and therapeutic intervention becomes overwhelmingly apparent. As with all interventions, one must be thoughtful about dosing, and how and when it is best introduced.

Clinical application of exercise as a therapeutic intervention for chronic pain

Understanding the tangible changes that occur in the nervous and endocrine systems following the development of chronic pain, clinicians can be better aware of the need for a tailored approach for the use of exercise in patient with chronic pain. Overall, the sensitivity of the nervous system for the patient with persistent pain requires a much slower and considered approach to exercise.

Graded activity and graded exposure for chronic pain

Graded activity, sometimes interchangeably referred to as graded exposure, is one of the key clinical translations of the understanding of pain science and how we use this science to underpin treatment for chronic pain. Used to improve functional deficits that have come about in the presence of chronic pain, it embraces simple principles that can be adapted to most situations.

Exploring functional losses

The loss and distress that most people with pain experience is frequently a combination of the presence of the pain itself, as well as the impact that the pain has on a person's life. Functional losses seen in the chronic pain setting can be as specific as a loss of range of motion in a single joint, and as broad as the lack of stamina required to sit at the dinner table and partake in a meal with friends or family. Graded activity is a set of principles used to first explore the functional deficits and set a program of exposure-based exercises or activities designed to address the deficits.

Difference between graded exposure and graded activity

Graded activity refers to a program of activity that positively reinforces patient activity levels. Graded exposure involves a confrontation element whereby patients are exposed or challenged with concepts, situations, or movements that they are fearful of. Both approaches have been shown to be effective in improving function in the rehabilitation setting, however, graded exposure has been demonstrated to reduce catastrophizing as well as improve function [52].

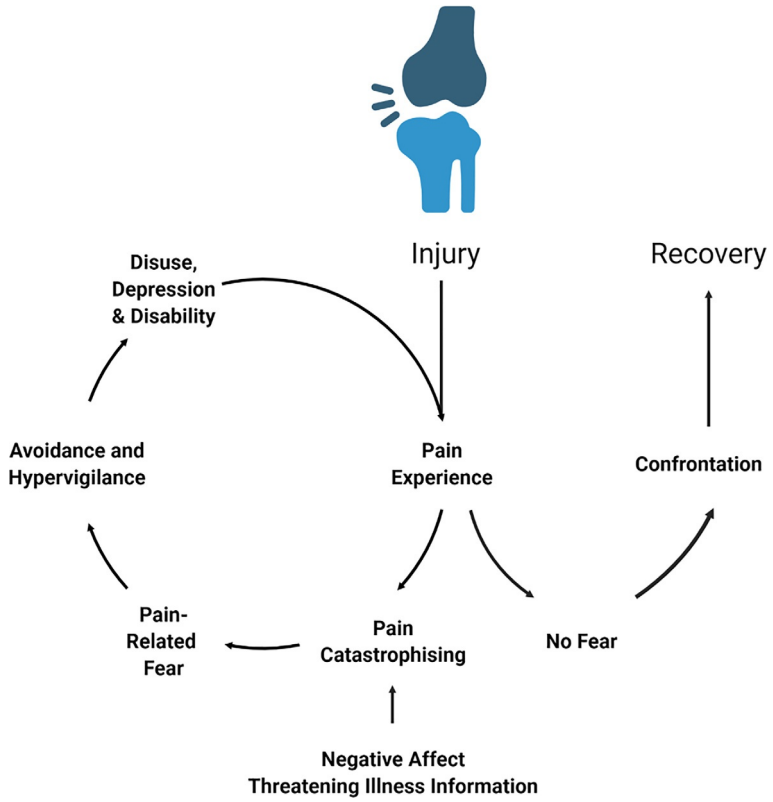


FIG. 5 Fear-avoidance cycle. *Adapted from Vlaeyen and Linton [7].*

Setting a graded exposure program

Prior to setting any form of exposure program, the practitioner needs to have spent adequate time listening to a patient's story, paying particular attention to their fears about the presence of pain and the meaning that they attach to the pain. Without having this understanding, it is possible that the best-planned exercise program may fail if patient fears have not been addressed. A common example of this is the patient who believes that the presence of pain during movement is associated with tissue damage or the potential to worsen an injury. The understandable behavioral consequences of holding these beliefs are a tendency to avoid movements or activities that cause pain. This avoidance often leads to deconditioning or further loss of function and a lowering of stamina. This cycle is referred to as the Fear-Avoidance cycle (Fig. 5) [53].

Allowing a patient to verbalize these fears can give them the sense that the practitioner has heard their concerns and can guide the practitioner in tailoring education material to provide maximum reassurance without invalidating their experience. Once these concerns have been acknowledged and validated as being very natural and common fears, the practitioner can then deliver information pertaining to chronic pain physiology. Also known as pain education or pain neurophysiology education (PNE), the aim of explaining this information to a patient is threefold:

- To separate pain from tissue damage
- To take the emphasis off pain and guide the patient to focus more on function
- To give a physiological explanation for a graded exposure approach

As covered in the earlier material regarding pain physiology, once the pain has progressed from acute to become chronic, there is less emphasis on inflammatory processes and tissue damage, and greater recognition of both central and peripheral sensitization. In de-threatening the presence of pain with pain education, practitioners can allow patients to better engage with exercise approaches knowing that they are not causing harm. As a single treatment entity for chronic pain, pain education or PNE has demonstrated small effect sizes in increasing function and reducing pain catastrophizing [54–56]. This is unlikely on its own to change the trajectory of a pain condition for an individual, however, it can be incredibly helpful to lay a foundation for a patient to engage with self-management strategies including exercise.

Graded exposure principles

During the history-taking and listening phases of the consult, a practitioner can gain a good sense of the functional losses that have occurred with the presence of pain. They can also get an understanding of what is important to the patient with regard to their rehabilitation goals. A good way to phrase the questions to explore these goals might include questions such as:

- If you had a magic wand and pain was not such a big deal for you, how would life be different?
- What things have pain taken away from you that you would like to work on getting back to doing again?

You will notice that these questions deliberately avoid discussing taking away or reducing pain and put the emphasis on function—the functional losses that are upsetting for the patient and the functional goals that they would like to work toward. This is an important distinction as a graded exposure approach does not aim to reduce pain, but rather to reduce disability and improve function. Once the patient has identified the functional goals that they would like to work on, a set of principles are applied to this task. These can include:

1. Finding a baseline of activity that does not provoke excessive pain either during the activity or in the 24 h following the activity.
2. Setting a schedule of activity or exercises that starts with this baseline and is practiced regularly.
3. Gradually increasing the parameters of this activity is a scheduled, graded fashion. These increases should be set collaboratively with the patient and practitioner and should be scaled up on a timed schedule, rather than focusing on how the patient is feeling during the exercise. The reason for this approach is that in a sensitized system in a chronic pain patient, moment-to-moment feedback from the body during exercise is often not as accurate as might be seen in a healthy person. Therefore, relying on this information to make decisions about the level of exercise can potentially either cause a patient to do too much or not enough exercise. Sticking to scheduled increases reduces this possibility. Increases of the exercise parameters may include increases to the overall time spent exercising, average heart rate, distance, weights, repetitions, or resistance. In some instances, the scheduled increases may involve different parameters at different times. For example, in a walking program, an initial grading up of the program may be to increase the time spent walking. At a later date, the grading up may be to add a slight incline on a treadmill session. The baseline activity should be sub-maximal and gradations should be small, aiming to remain sub-maximal as capacity increases. In the event that a grading up of the exercise causes significant increases in pain levels in a 24-h time period following the exercise, it is likely that the increase was either too early or too large for the patient at that time. The patient should be reassured about the temporary nature of these flare-ups and a flare-up self-management plan can be enacted to help a patient to cope with the increased pain levels until they settle. Subsequent graded increases to the program should be adjusted down with reference to this reaction. The principles of such an approach need to be explained to patients well, as many patients will either tend to err on the side of "boom and bust" attitudes (if 10 squats is good then 50 must be better) or can be too cautious and under-dose a program (it hurts so I should be careful and stop doing that exercise). A simple guide to explain this might be—on a good day do not do more, and on a bad day try doing half or a quarter of the exercises, rather than choosing to do none. This way, a level of consistency in a program can be better achieved with fewer flare-ups and gentle experiential exposure to movement in the presence of pain, which can be a powerful way to reduce a fear-avoidance cycle.

Self-efficacy

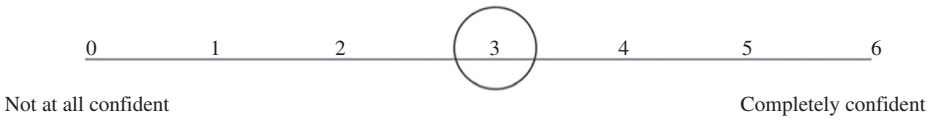
The role of self-efficacy has been identified by researchers and clinicians as an important factor in the development and maintenance of chronic pain for some time. Defined as the subjective confidence in one's own ability to achieve a task in 1977 by Bandura [57], this psychological construct has been shown to be more predictive of the development of chronic pain than any physical factors such as biomechanics, load, posture, or levels of tissue damage [7]. People who have high self-efficacy tend to have greater confidence in their ability to manage their musculoskeletal pain and are more willing to persist in the presence of setbacks. For the person with pain, this means they are more likely to attempt tasks in the presence of pain and tend to be less worried about the presence of pain. According to the research, this mental resilience seems to be a strong protective factor in the progression of acute pain to chronic pain and disability. Additionally, people with high self-efficacy do not seem to be as distressed or depressed as people with low self-efficacy and will generally have less pain (as rated by VAS scores) [58]. Understanding these concepts, as clinicians, we have an opportunity to detect the presence of low self-efficacy in our patients and direct our treatment accordingly.

Pain Self-Efficacy Questionnaire—Two-Item Short Form (PSEQ-2)

Michael K. Nicholas, PhD, Brian E. McGuire, PhD, and Ali Asghari, PhD

Please rate how **confident** you are that you can do the following things at present, **despite the pain**. To indicate your answer circle one of the numbers on the scale under each item, where 0 = not at all confident and 6 = completely confident.

For example:



Remember, this questionnaire is not asking whether or not you have been doing these things, but rather **how confident you are that you can do them at present,** despite the pain

1. I can do some form of work, despite the pain ("work" includes housework and paid and unpaid work).	0 Not at all confident	1	2	3	4	5	6 Completely confident
2. I can live a normal lifestyle, despite the pain.	0 Not at all confident	1	2	3	4	5	6 Completely confident

FIG. 6 The Pain Self-Efficacy Questionnaire-2 (PSEQ-2).

Measuring self-efficacy can be done using the Pain Self-Efficacy Questionnaire (PSEQ) [59] or its shorter cousin the PSEQ-2 (Fig. 6) [60], both demonstrated to be valid and reliable tools. The PSEQ-2 consists of two questions and asks the person to rank on a scale of 0–6, 0 being not confident at all, and 6 being completely confident they can complete activities and live a normal lifestyle in the presence of pain. Scores of 8 out of a total of 12 are considered to indicate a desirable level of pain self-efficacy and are likely to indicate that a patient is better placed to recover, compared to those who might score 5 or below.

Self-efficacy is an important construct to understand when setting exercise programs for patients with chronic pain. If someone has very low confidence in their body and is fearful of movements, situations, or activities, being aware of this and being able to measure it can be helpful when setting a graded exposure program. If they are starting treatment with a low PSEQ score, the things to keep in mind when setting an exercise program include:

- Reassurance in the form of pain education can reduce fear and allow patients to attempt new activities that they previously would have avoided.
- People with low self-efficacy often need higher levels of supervision when starting an exercise program. This allows for constant feedback and reassurance and for support and troubleshooting in the event of a pain flare-up.
- The baseline program should be set at a very low level, to begin with. The intentions in these early phases of an exercise program include:
  - Building a habit
  - Feeling a sense of success in completing the prescribed program
  - Building confidence in trying new movements and activities in a way that is unlikely to cause a flare-up.

Successfully starting and grading up an exercise program will naturally start to help increase a patient's self-efficacy as they are able to see the improvements and hopefully see it translate through to functional gains.

Managing pain flare-ups

Anyone trying activities that they haven't done in some time is likely to experience a level of musculoskeletal pain. Many people returning to their gym after a long break or picking up a tennis racquet for the first time in years can attest to this. Our tendency is often to expect to be able to pick up where we left off the last time, we did that activity. Unfortunately, this often

leads to several days of being stiff and sore. For the chronic pain patient with a highly sensitized nervous system, new activities, or increasing the load of existing activities can easily cause a pain flare-up. Most patients would describe this experience as a temporary increase in their familiar pain. It will usually tend to occur in the hours following the exercise or the next day and can last for several days to weeks. Often these extreme pain levels are vastly disproportionate to what would be seen in a person who does not suffer chronic pain. The physiological mechanisms that are responsible for such disproportionate increases in pain levels most likely lie with both peripheral and central sensitivity changes, including reductions in descending inhibitory modulation mechanisms. A nociceptive driver may or may not be able to be identified for the individual situation, but the nervous system changes enhance and exaggerate this response [61]. This information has two important follow-ons.

Firstly, regardless of the presence or absence of inflammation or other local tissue factors that may be related to the pain experience, whatever the patient is describing their pain is what clinicians should be tuning into and believing. It is very common for chronic pain patients to have a flare-up of pain following some form of mild physical activity and it is frequent that these experiences are dismissed by health practitioners as being not real, not possible, all in the persons head or a variety of other dismissive and invalidating responses. This invalidation can be crushing for the patient in pain, who is dealing not only with the distress of high pain levels but also the sense of not being believed.

Secondly, physiology reminds us that even though the pain is real and often distressing, the heightened response is due to the nervous system changes and not due to tissue damage. Reminding patients about this in preparation for their first flare-up when starting any movement program can help to reduce the distress associated with the presence of flare-up pain.

Creating a flare-up management plan

Knowing that flare-ups are possible once we start engaging with different movements, activities, or altered loads of existing exercises, it can be helpful to have a pre-prepared flare-up management plan to help reduce the distress associated with a flare-up. In preparing such a plan collaboratively with a patient, we are setting expectations that times of increased pain are normal and somewhat expected as we try new things. Additionally, we can pre-arm them with reassurance of a couple of helpful principles for managing flare-ups. These include:

- This is temporary and will pass
- The tissues have not experienced damage
- There are some things that I can do to help myself to allow this to pass quicker and reduce the distress that I feel in the presence of the flare-up

Working with the patient, it can be helpful to create a written list to refer to in the presence of high levels of pain. The reason it is preferable to have a written list is that frequently during a flare-up, patients may also experience high levels of distress, and while in pain, their capacity to logically recall the information may be reduced. Therefore, having a "go-to" list can help patients engage with active self-management strategies and be less tempted to resort to passive approaches such as medication or healthcare seeking. When creating this list, it can be helpful to write the dot points above at the top of the list as a reminder and orientation. You can then collaboratively create a list of seven or more things that are known to the patient to reduce either their pain levels or distress levels, even if these strategies are temporary. The idea is that the patient will systematically go through the list and attempt each of the strategies. Each strategy may only reduce pain or distress by a small percentage but the act of trying serves as a great self-efficacy boosting exercise as the intention is "I am trying to help myself." Once they have completed the series of tasks, if they are still in a high level of pain and distress, they can repeat the list.

Some options that patients have found helpful include:

- Heat packs
- Hot Showers (10 min or more at a high temperature over the painful regions)
- Mindfulness or relaxation exercises
- Calling a friend for a chat
- Watching a funny TV show or YouTube comedy
- Looking at photos that make you happy
- Going for a short walk
- Making a nice cup of tea or coffee
- Listening to a favorite piece of music
- Writing/journaling

- Creative expressions or hobbies
- Sitting in the sun or nature (sunscreen on!)
- Self-massage
- Stretching exercises
- Cuddles on the couch with a partner or child
- Reading

Prompting the creation of the list might involve suggesting to the patient: what are things that make you feel relaxed, feel nice, reduce your pain a bit or lift your mood? It is important to set the expectations that these will not take the pain away completely, but should reliably reduce the pain a small amount, which is often enough to be able to better cope with the pain.

Examples of graded exposure programs

Many exercise programs fail because the patient and practitioner are not successful in identifying the baseline. Most commonly what is seen is the program being set too high with subsequent excessive pain, frustration, and abandoning of the program. For patients with significant central sensitization, the starting point of an exercise program may be very low. It is important to normalize this as part of the process as this low entry point could be viewed as being ineffective or tokenistic. Explaining to the patient that these early starting exercises are designed to build habits around exercise as well as confidence in the body to achieve these movements, is important to help with adherence to a program.

Widespread body pain

Sometimes referred to as fibromyalgia, widespread body pain presents with diffuse, chronic musculoskeletal pain, fatigue, headaches, sleep disorders, and cognitive and psychological disorders [62,63]. Various types of exercise used to treat fibromyalgia have been shown to be effective in improving overall well-being, increasing function, decreasing pain, and improving depressive symptoms. These include strength training, moderate-intensity aerobic training, hydrotherapy, and tai chi [64]. In healthy individuals, central nervous system mechanisms exist to reduce sensitivity to pain during and following exercise. These mechanisms are known as exercise-induced hypo-algesia (EIH). EIH is frequently impaired in people with chronic pain, particularly widespread body pain. This means that where healthy individuals may feel a sense of well-being and reductions in pain following exercise, many people with widespread body pain may not experience any reductions in pain sensitivity or may even experience an increase in pain sensitivity. This is thought to be related to changes in either the endogenous opioid, endocannabinoid, or serotonergic systems seen in chronic pain states [65,66]. The problem that this presents is that exercise is known to be beneficial for people with widespread body pain, however, there is a chance that pain may feel worse, not better in the short-term following exercise. This is an obvious disincentive to maintaining an exercise program designed to address widespread pain. The answer to addressing this paradox for the patient with widespread pain most likely lies in education and expectation setting around these concepts and then ensuring that the baseline starting points of the graded exposure program are low enough not to cause excessive amounts of pain following exercise. This may mean that the starting points for such a program are very low and grading them up is equally much slower than in other settings.

Headaches

One of the most important factors in directing treatment for the chronic headache patient is a diagnosis. The efficacy of treatment is dependent on tailoring the treatment to the specific type of headache presentation. To familiarize yourself with the common presenting signs and symptoms of the most common headaches, it is advisable to refer to the International Classification of Headache Disorders (ICHD) [67]. The three most common and distinct types of headaches seen in practice include migraine, tension-type headache, and cervicogenic headache. Each has quite a different etiology and as such, treatment approaches differ.

Migraine

Migraine headaches tend to respond well to exercise. The type of exercise and the appropriate dose remains to be tightly identified in the literature, however, there is moderate level evidence to suggest that aerobic exercise can reduce the number of headache days over a period of time, compared to no exercise control group [68]. It should be noted that most migraine sufferers will find that exercise during a migraine will tend to exacerbate the symptoms. Due to the lack of strong evidence

pointing toward a particular type of exercise being overwhelmingly more effective than others, tailoring an exercise program for migraine patients should take into account their preferences and likelihood of continuity.

Tension-type headache

This common type of headache does not generally respond well to a single modality treatment approach. There is not a great deal of high-quality evidence to suggest that a specific type of exercise gives consistent positive outcomes. A multi-modal approach to treating this type of headache is generally considered to be the best approach. This might include medication, relaxation strategies, cognitive behavioral therapy, and exercise. It is likely that exercise in this setting would be helpful to increase overall stamina and to help facilitate descending inhibitory mechanisms [69].

Cervicogenic headache

This headache could be better conceptualized as mechanical neck pain which happens to refer to pain in the head. Sensory information from the upper three cervical spinal nerve roots is believed to interact with sensory nerve fibers in the descending tract for the trigeminal nerve in a region of the upper cervical spinal cord. It is believed that due to the close nature of the nerve pathways, a level of functional convergence may occur. This means that a bidirectional referral of painful sensations between the areas supplied by the nerves is possible. Therefore pain from the upper neck structures may be felt in the head [70]. There is a moderate level of evidence to suggest that specific neck exercises can be beneficial in the treatment of cervicogenic type headaches [70–72]. Most of these studies have focused on specific activation of deep cervical flexor musculature.

Neck and back pain

Evidence around the efficacy of the use of exercise for treating back and neck pain has been highlighted in the literature for many years. Narrow focus on the type of exercise, such as motor control exercises, pilates, resistance training, and aerobic training dominated the bulk of the research produced for many years and as such, recommendations for these types of exercises were generated in many of the guidelines for the treatment of low back pain at that time. As the research has evolved, not only have these more localized or specific types of exercises been demonstrated to be helpful in both improving function and decreasing pain, but other, simpler, and more accessible types of exercise such as walking have proven to be effective [72–74]. As we move toward better implementation of our understanding of the biopsychosocial context of common conditions like neck and back pain, so too has our application of the research regarding the efficacy of exercise treatment of these conditions. As such, many of the guidelines created for both acute and chronic low back pain place greater emphasis on exercise approaches being aimed at increasing movement levels in a way that is tailored to what the patient is likely to be able to engage with in both the short and long term [75].

Neuropathic pain

Neuropathic pain, most often described by patients as having sharp, shooting, burning, or electric shock qualities is among the most debilitating chronic pain presentations. Physiological evidence for the use of exercise in treating neuropathic pain exists, particularly the role of exercise in modulating maladaptive neuro-inflammatory changes [76–78]. Movement in various forms is frequently used in the treatment of neuropathic pain with the intention of both reducing pains and improving function. When patients are using neuropathic descriptors for their pain, it is usual for the starting point for an exercise program to be considerably lower than for more general chronic musculoskeletal conditions. In the presence of these neuropathic descriptors, as well as clinical evidence of neuropathic pain such as allodynia and hyperalgesia, it is likely that the point at which a flare-up of pain comes on may be much lower than patients without neuropathic descriptors. Therefore, when starting an exercise program for such patients it is advisable to start at a very low baseline and build up slowly according to the response. Frequent flare-ups are common in this pain population and pitching exercise at an appropriate level can be difficult to achieve. In some cases, maintaining function may be the ultimate goal whereas improving function is found to be hampered by low physical thresholds and frequent flare-ups.

Chronic pelvic pain

Chronic pelvic pain (CPP) in men and women can occur throughout various stages of life and present with varying symptoms. There is little high-quality evidence to direct exercise treatment of chronic pelvic pain [79]. There is a small amount of evidence to suggest that exercise such as yoga, stretching, dancing or aerobic training may provide good

reductions in menstrual pain in females with dysmenorrhea. Participants in the studies reviewed in a recent Cochrane review exercised for 45–60 min, three times a week to achieve the clinically relevant reductions in pain [79].

Prescribing exercise for chronic pain

The role of exercise in the management of chronic pain is both direct and indirect. Direct in that it can have small to moderate positive effects on pain, and indirect, in that it can be a form of graded activity, and it can enhance general health on both physiological and psychological levels. Exercise demonstrates the potential to be beneficial in a variety of chronic pain conditions and is both low cost and accessible. Exercise instruction can be delivered effectively one to one, in small group settings, or via telehealth, making it a viable intervention across a range of clinical settings. Though it has good clinical utility, there are some barriers to uptake of exercise prescription. One such barrier is that many people report an increase in their pain intensity post-exercise, this is typically transient in the short term, but a significant barrier we must overcome. Previously in the chapter, we addressed strategies to help reframe the intention and expectation of undertaking an exercise program for sufferers of chronic pain. We will now explore some more practical aspects of exercise prescription, from establishing a baseline, to monitoring intensity and progression.

Effectiveness of exercise as an intervention for chronic pain

There is an abundance of clinical and epidemiological literature demonstrating the positive effects of exercise on numerous aspects of health, from all-cause mortality to QOL, physical function, and onset/progression of chronic disease states [80]. Health departments around the world acknowledge these benefits, with many having specific physical activity guidelines in place. These guidelines, despite small regional differences, encourage regular physical activity, daily, if possible, of varying intensities (moderate to intense) and modalities (cardiovascular and resistance training) [81]. Chronic pain patients as much as any other population need these benefits to limit and counter the effects of chronic pain but this does not mean that exercise can therefore be considered an effective intervention for chronic pain. Certainly not in isolation. Being that chronic pain is a whole-person condition, not limited to one body system or aspect of life, very few individual interventions have significant and/or lasting effects on pain. As a result, current best practice is to incorporate a multi-disciplinary management approach that layers in several strategies and allows for summation of effects [82]. To this end, exercise can be considered a positive general health intervention, which may provide improvements in chronic pain, to some degree, in some people. The critical questions are then what exercise or activity, how much, and in who?

A large Cochrane review assessed the effect of exercise on chronic non-cancer pain in adults aged >18 years [11]. It included randomized controlled trials assessing exercise/physical activity as the primary intervention and the primary outcome measured was pain. Secondary outcomes assessed included physical function, psychological function, quality of life, adherence to the prescribed intervention, healthcare use/attendance, adverse events (excluding death), and death. The review included papers looking at a variety of chronic pain presentations and included a variety of exercise interventions. The majority of participants were deemed to have mild to moderate pain at baseline, and the following outcomes were observed:

- three reviews found no statistically significant effect on pain
- three reviews found at least a 30% reduction in pain
- seven reviews found approx. 10%–20% reduction in pain
- seven reviews found statistically, but not clinically significant reductions in pain

The paper concluded that "Overall, results were inconsistent across interventions and follow-up, as exercise did not consistently bring about a change (positive or negative) in self-reported pain scores at any single point." Additionally, the authors noted the following:

- Importantly and promisingly, none of the physical and activity interventions assessed appeared to cause harm to the participants, with most adverse events being increased soreness or muscle pain, which reportedly subsided after several weeks of the intervention.
- None of the included reviews examined generalized or widespread chronic pain as a global condition, each instead examined specific conditions that included chronic pain as a symptom or result of the ongoing condition (e.g., rheumatoid arthritis, osteoarthritis, low back pain, dysmenorrhea, etc.)

- There is limited evidence of improvement in pain severity as a result of exercise. There is some evidence of improved physical function and a variable effect on both psychological function and quality of life. However, results are inconsistent, and the evidence is low quality (tier three).
- For clinicians and people with chronic pain, the evidence in this overview suggests that the broad spectrum of physical activity and exercise interventions assessed here (aerobic, strength, flexibility, core training, etc.) are potentially beneficial, though the evidence for benefit is low quality and inconsistent.
- Physical activity and exercise may improve pain severity as well as physical function and quality of life.

This review provides a good overview of the current literature on exercise for chronic pain, which suggests there is a likely small to moderate benefit on pain, independent of the type of exercise, for a variety of painful presentations. It also notes that there is potentially no effect of exercise on pain in some circumstances. What this review does not tell us, is whether certain pain conditions respond more favorably to certain types and/or dosages of exercise. Nor does it provide any insight into the individual factors that may be predictive of a positive response to exercise as an intervention for pain. The other question that remains, is whether exercise is beneficial for those who suffer from chronic primary pain—i.e., pain that is not attributable to another condition, including widespread/multi-site pain.

Potential mechanisms of exercise for pain

As discussed earlier in the chapter, chronic pain is a multi-system condition, with both bottom-up and top-down influences. Just as the entire process of pain is not fully understood, neither are the mechanisms by which exercise can influence pain. The majority of these proposed mechanisms are based on empirical observation, foundational science, and small clinical trials. As such, they are subject to change over time as new knowledge emerges.

Descending modulation

Descending or central modulation was described earlier in the chapter. Exercise shows signs of influencing modulation of nociception at both spinal and supraspinal levels, resulting in the release of inhibitory factors like endogenous opioids, GABA, and serotonin. One consideration that is relevant for chronic pain patients is that for some, descending modulation is impaired, and thus applying a systemic stressor like exercise, results in flare-ups, no matter the dose. While rare, it should be acknowledged that this condition does exist and not everyone can tolerate, let alone benefit from exercise for chronic pain [83].

Anti-inflammatory effects

Both peripheral and central sensitization of neurons occurs in association with acute and chronic inflammatory processes. Exercise is hypothesized to positively affect chronic inflammation by activation of anti-inflammatory substances, like tumor necrosis factor (TNF), interleukins, T-cells, and various other immune-modulatory cytokines [84,85].

Autonomic regulation

The autonomic nervous system works to regulate many of the automatic functions of the body. Autonomic dysregulation is associated with chronic pain, typically in the form of increased sympathetic activation (i.e., chronic stress response). Regular exercise is associated with improved autonomic regulation [86].

Mechanotransduction

Mechanotransduction defines the process by which biological cells convert mechanical forces into electrical or chemical processes. Exercise involves production and absorption of forces by the neuro-musculoskeletal system, which has widespread physiological effects. These effects may indirectly influence pain via both peripheral and central mechanisms, including but not limited to endocrine signaling and protein synthesis which may aid tissue remodeling and, influence peripheral inputs to the central nervous system [86].

Neurotrophic factors

Chronic pain is associated with cognitive decline, including the onset of dementia. This may indicate some form of chronic neurogenic inflammation, impacting neuronal cell function, growth, and repair. Exercise is known to stimulate endogenous production of brain-derived neurotrophic factor (BDNF), which helps regulate neuronal growth and repair [87,88].

Although we describe potential mechanisms by which exercise may help modulate pain, it would be remiss to not mention that for practical purposes, these things happen simultaneously. Therefore, regardless of the actual mechanisms, the benefits of exercising for chronic pain come from starting and gradually progressing in a manner that is safe and within an individual's present tolerance for adaptation. This is discussed in further detail below.

Getting started

Using exercise as an intervention for chronic pain poses a number of challenges across multiple domains. These include, but are not limited to:

- Whether somebody starts an exercise program (compliance)
- Whether somebody continues with an exercise program long enough to see positive outcomes (adherence)
- The type of exercise
- The dosage (volume/intensity/frequency)
- Initial health status (physiological and psychological)
- Socio-economic factors

To overcome these challenges, especially with a body of evidence that is inconclusive as to what is the optimal approach to using exercise as an intervention for chronic pain, a practical, patient-centered approach can be used to guide clinical decision-making.

Addressing compliance

Anecdotally, clinicians will often claim they have suggested exercise, but a patient/client has not been compliant with their recommendations. Additionally, patients themselves often cite lack of time or motivation for not beginning or adhering to an exercise program. Both of these statements and the thinking behind them are suggestive of a very unidimensional approach to behavior change that is more practitioner-centered than patient-centered, and less likely to succeed.

This has been supported in qualitative studies on the topic [89]:

> The results of this study suggest that in this sample, exercise adherence is not simply the patients lacking motivation or not having enough time in the day.
>
> Instead, the results suggest that adherence to prescribed exercise is the product of chiropractors' and patients' experiences and beliefs, the development of their clinical relationship, and the way exercise is prescribed and monitored in parallel with other treatment modalities.

While this study looked at Canadian chiropractors specifically, a similar pattern presents across multiple allied health professions and nations [89]. In the work cited above, the authors have outlined *enablers* and *barriers* to help engage people in positive behavior change, specifically as it relates to exercise prescription. These are outlined in Table 3.

When multiple variables relating to compliance are considered, we can develop the opinion that no single factor will lead to compliance for the majority of people. Thus, health professionals must understand how to implement

TABLE 3 Common enablers and barriers to exercise in people with chronic pain.

Enablers
Participants feeling involved in the process
Supervision
Pain control
Knowledge acquisition (via information sharing)
Goal sharing
Follow-up contact
Barriers
Perception of what exercise is
Lack of time
Diagnostic uncertainty
Fear of pain
Lack of fit into daily life

behavioral change strategies, in order for patients to gain the benefits of undertaking an exercise program for chronic pain [89–91].

Behavior change basics

Human behavior is complex. It is only when we view both individual and group behavior through a wider lens, we can start to make sense of it. Part of this wider lens is the effect of time on outcomes (e.g., people will smoke now because the adverse effects are delayed). Another part is the effect of meaning. Meaning becomes more important when acting in the face of both uncertainty and suffering—such as that encountered when beginning an exercise program as a treatment for chronic pain. An example of this search for meaning in the face of suffering is the increased religious beliefs/behaviors demonstrated in those who suffer from chronic musculoskeletal pain [92].

To ensure the best chance of success in both starting (and continuing) an exercise program, a person needs the proposed action to have meaning that is both related to and independent of a potential outcome. That is, if the person is seeking reduced pain and increased function, these provide a superficial source of meaning for the activity, however, empirical evidence suggests that a deeper level of meaning is more robust at sustaining behavior change. To elicit meaning, motivational interviewing techniques can be used. This form of communication ticks off a number of enablers—feeling involved, goal sharing, and knowledge acquisition. By facilitating a patient to discover their meaning, or put another way, their motivation to change their actions, the likelihood of success is increased.

Increasing adherence

While meaning and motivation can help get someone started with a new activity, for long-term benefits, this activity needs to become habit-forming. There are a variety of techniques that have been discussed to increase adherence in both the short and longer term [93]. Two examples are outlined below:

- *Shrink the change*
  By reducing the actual (or perceived) size of the change (new activity), the task becomes more achievable in the short term. With exercise for pain, a graded approach is optimal, and this fits in well with the concept of "shrink the change." In the beginning, a smaller amount of exercise is needed to elicit positive adaptations. This can gradually be built upon.
- *Anchor the activity*
  This refers to attaching the activity to something that is already habitual. For example, if someone was recommended to do some leg strengthening exercises daily, and they drank tea twice a day, they could perform a set of exercises while they waited for the tea to brew.

The most important concept in behavior change is for both parties to acknowledge that it relies on more than discipline and that setbacks are a normal experience, and should be planned for as to not create feelings of failure and despair. These strategies serve to develop habits, which are explored in goal-setting below.

Goal setting

Goal setting is a method of defining desired outcomes with a view toward orientating behaviors toward achieving the said outcome. In essence, it is a way to develop a "roadmap" to a specific achievement or state. One widely accepted way to set goals is the SMART approach. This stands for *Specific, Measurable, Attainable, Realistic, Timely*. The idea being, that when a goal has these attributes, it is more likely to be achieved. An example of a SMART goal is "I would like to have $1000 saved in 3 months." Compare this to a non-SMART goal, which is vague and has no timeline "I would like to save more money."

Applying SMART goal setting to chronic pain management

For a sufferer of chronic pain, goal setting can seem futile, especially when the desired goal might be "to have no pain". Yet this may not be realistic for many, nor does it do anything to help guide the actions one is required to take in order to achieve this. For many chronic pain sufferers, their pain has significant impacts on function, and this is where exercise can be a vital tool toward optimal pain management. Thus, making goals functional, rather than pain-focused, will typically yield better outcomes in terms of quality-of-life improvements.

An example of a SMART, functional goal for a chronic pain sufferer could be:

"I would like to increase my ability to walk for a time by 15% in 6 months".

This goal is specific—increase the ability to walk, measurable—by 15% above baseline, achievable—this rate of improvement is possible (depending on various factors), whether this is realistic depends on the baseline status, but for an able-bodied person with chronic pain this is often possible, timely—it has a defined period.

From goals to skills

The biggest limitation of setting goals, even if they are SMART, is it does not help inform you about how to achieve them. In order to achieve a certain goal, actions must be taken. These actions or behaviors should become habits. These habits should develop skills or attributes that will build toward achieving the desired goal. Continuing with the goal of increasing walking time by 15% in 6 months, we can break the goal down into certain attributes required:

- Mobility
- Balance
- Leg strength
- Cardiovascular endurance
- Psychological resilience

Based on an individual assessment (discussed later in the chapter), the areas that need the most improvement can be addressed by implementing certain behaviors. In this case, the behaviors will be in the form of exercises. Setting a SMART goal is only the first step toward actually achieving that goal.

Having a reason (meaning) for wanting to achieve that goal provides a powerful motivational tool to draw on when things are challenging—as is inevitable with any process of achievement. This can help with consistently implementing the behaviors required to develop the skills and attributes needed to achieve the goal.

Prognostic factors

When discussing exercise for pain as a management strategy, and during the goal-setting process, prognostic factors should be addressed. The following factors are associated with a higher response to exercise [94]:

- Baseline pain intensity
- Mental health status
- Age
- Prior treatment
- Drug use

In a prospective study, patients were assessed at baseline and underwent six sessions of physiotherapy exercises and education over consecutive days. The exercise programs were individualized and delivered under supervision. Follow-up assessments were conducted at discharge and 1 year. The only variable associated with a better outcome at discharge was baseline pain intensity—high pain was associated with a worse outcome. Over the long term, younger age, better baseline mental health, less prior treatments, and drug usage were associated with better outcomes at 1 year follow-up. Interestingly, the is a very low correlation between improvements in physical qualities like strength, endurance, and flexibility and improvements in pain [94]. This has been studied for a variety of clinical pain presentations.

Baseline assessment

The baseline assessment should be designed to give enough insights as to the current status of the individual's health, fitness, and psychology in order to guide the initial program design and gauge improvements in follow-up assessments. An ideal assessment is comprehensive in what information it provides, but concise and practical—that is, it does not require expensive or rare equipment to perform.

Assessments can include:

- Validated outcome measures
- Quantitative physical assessments
- Qualitative physical assessments
- Self-reported evaluation

Considering the wide variety of factors that can influence exercise prescription, along with potential and likely outcomes, it is optimal to utilize a broad range of assessments across multiple systems and domains. Specific examples of assessments from each category include, but are not limited to:

Validated outcome measures:

- *Psycho-social factors*: Identification of yellow flags, Pain Catastrophizing Scale, Fear-Avoidance Scale, K10 (mental health screening).
- Regional specific outcome measures (knee, low back, upper limb, etc.).
- Functional outcome measures (patient-specific functional scale, back pain functional scale, etc.).

Quantitative physical assessment:

- *Vital signs*: Age, height, weight, blood pressure, pulse, respiratory rate.
- Neuro-musculoskeletal testing (range of motion, force output testing, etc.).
- Validated physical tests (sit to stand, 6-min walk, etc.).
- Quantified movement screening (Y-balance test, hop test index).

Qualitative physical assessment:

- Functional tasks (ability of patient to comfortably perform a particular task)

The assessment(s) should reveal the factors you need to influence, and then be able to measure relevant change. It should also identify the current functional capacity of the patient/client, in order to guide the starting point of their exercise program. It is important to note, that it's rarely a single factor, but rather the unique interaction of all factors in that environment. The person should be the focus of the exercise program, not the results of the assessment.

Types of exercise

Before discussing which types of exercise are optimal for those suffering from chronic pain, a brief clarification of commonly used terms is needed.

Physical activity: Physical activity is defined as any bodily movement produced by skeletal muscles that require energy expenditure. By definition, all physical activity is movement, but not all physical activity is exercise.

Movement: Go in a specified direction or manner; change position, change the place, position, or state of.

Exercise: Activity requiring physical effort, carried out to sustain or improve health and fitness. An activity carried out for a specific purpose. Exercise is a sub-category of physical activity that is planned, structured, repetitive, and aims to improve or maintain one or more components of physical fitness. Exercise comes in many varieties, but for the sake of simplicity, we can broadly categorize exercise into four main groups:

1. *Cardiovascular exercise* (cyclic endurance activities such as walking, running, cycling, rowing, etc.) primarily leads to adaptations in the cardiorespiratory system
2. *Resistance training* (exercise that involves overcoming resistance, be it bodyweight, or external load, includes weightlifting, pilates) which primarily leads to adaptations in the neuromuscular and skeletal systems
3. *Flexibility training* (exercises that involve movement or positions that take joints through to their end range of motion, including stretching, yoga) which primarily leads to adaptations in the neuromuscular and skeletal systems, though these are different from those gained from resistance training
4. *Sports and skill-based activities*

Sports and skill-based activities typically involve a composite of the three generalized classes of exercise described. However, they are also typically open and chaotic versus closed or controlled, which means there is a high degree of random variability in many sports activities. While enjoyable, these do not make for an easily scalable or progressive approach, and thus are not optimal for managing chronic pain. Thus, we will exclude sports and skill-based activities from the discussion for the sake of clarity and brevity.

Is one form of exercise superior for pain relief?/What type of exercise should be performed?

Most studies comparing exercise modalities for pain management do show clear superiority/inferiority. In practical terms, an exercise program that incorporates aspects of all three exercise categories gives exposure to multiple mechanisms of action for pain management, as well as build broad physical qualities than enhance resilience and adaptability. Working

toward the national guidelines for physical activity, which recommend a blend of low-moderate activity/exercise, as well as higher intensity activity/exercise and muscle-strengthening (resistance) activities/exercise is a very good target, as it promotes overall health and longevity, in addition to pain management.

While many people have a preference for one particular form of exercise, there are clear benefits to be had from engaging in these different categories/forms of exercise. So, while something is generally better than nothing, and what is preferred is more likely to get done consistently, for maximal/optimal benefit, we stand by the above approach.

Dosage and progression

Dosage and progression are important, as it relates to performing enough exercise to create a positive physiological or psychological response. Dosage also involves overall load management, with aim of minimizing the risk of significant adverse effects from exercise—pain flare-ups, soreness, fatigue, etc.

Exercise dosage can be broken down into two key components:

1. Intensity: measured as a percentage of maximum output
2. Volume: measured as total amount of work performed

These two components can be viewed from an individual session perspective, or over a longer period (weeks/months). When prescribing exercise for chronic pain, the aim is not to maximize performance, but gradually increase physical capacity, facilitate endogenous analgesic processes and provide a positive psycho-emotional experience. With this in mind, dosage does not need to be as strictly prescriptive as a typical performance-focused exercise program. In fact, there is evidence supporting self-dosage in terms of both intensity and volume results in similar physiological improvements, with a more positive affective experience for participants.

Practically, because pain fluctuates, combining self-dosage with an overall plan for each session, along with the macro progression over time allows an individual to have an internal locus of control, with enough external structure to account for these fluctuations in pain and fatigue. We will discuss how to monitor intensity/volume shortly. Applying this approach to exercise progression, while not the only way a more flexible approach tends to account for potential flare-ups, while still ensuring that over time, positive adaptation takes place. In certain circumstances, a more prescriptive approach is beneficial, however, this is dictated more by clinical experience along with trial and error, versus any definitive literature on the topic.

Managing intensity

There are two main ways to monitor exercise intensity:

1. Subjective, using a *rating of perceived exertion (RPE)* scale
2. Objective/quantified, using external sensors/monitors (heart rate monitors, GPS sensors, power meters, etc.)

RPE correlates well with measured heart rate, power output, and velocity, and requires no specialized equipment. Additionally, RPE is an established and reliable measure of exercise intensity for both aerobic exercise and resistance training [95]. While using objective data can be quite helpful in measuring exercise output and progression, when it comes to pain, improvements in physiological characteristics, like strength, endurance, and flexibility are poorly correlated to pain improvements [96]. Accordingly, this chapter will focus on how to use RPE in a graded exercise program for chronic pain management.

Rating of perceived exertion

RPE is measured according to two main scales, first described by Gunnar Borg (Table 4):

1. The 6–20 numerically rated from 6 to 20 and is designed to reflect estimated heart rate (multiply by 10)
2. The second is scaled from 1 to 10 for ease of use

Applying RPE to an exercise program for chronic pain

Exercise intensity is the key variable to manage when prescribing exercise. Intensity is described as the percentage of maximum, and as discussed, this correlates well with perceived exertion.

Intensity, by definition, will impact both volume and frequency. When initially prescribing exercise for pain, we need to account for both psychological and physiological factors and monitor for adverse effects.

TABLE 4 Borg RPE scale.

Borg RPE score	Level of exertion
6	No exertion at all
7	
7.5	Extremely light
8	
9	Very light
10	
11	Light
12	
13	Somewhat hard
14	
15	Hard (heavy)
16	
17	Very hard
18	
19	Extremely hard
20	Maximal exertion

For some, starting too slowly might be challenging, as it is perceived as too easy, or not doing anything; this can be addressed with appropriate education. For others, any form of exercise might be perceived as too intense. Education and expectation management are important factors that precede exercise prescription. A starting point of 7.5–11 on the 6–20 scale is a good general approach, as it facilitates adaptations and progressive increases in volume with minimal risks of adverse effects. There is no consensus on the optimal exercise intensity for pain management/relief, so it makes sense to start at comfortable intensity, and slowly progress, monitoring the response along the way.

How much exercise do you need?

There is much debate on how much exercise is optimal for pain management. Again, there is no clear consensus. In consideration, we refer back to the national physical activity guidelines as a goal to work toward. With that said, if someone is currently sedentary, be it due to their pain or otherwise, any amount of exercise will yield a benefit. Practically, encouraging people to start exercising, even if they do not achieve the recommended physical activity guidelines is one of the best things that can be done for both their individual health and public health at large [97]. To answer the question posed, the amount of exercise that is needed may differ from the amount that is realistically achievable, and our stance is as follows:

- Some exercise is better than no exercise
- More exercise is generally better, up to a point
- The national physical activity guidelines are a good goal to aim for in terms of total dosage

Practical aspects of dosage

Optimizing exercise dosage is a key variable to optimizing outcomes. There are numerous approaches to dosing exercise. Traditionally, for resistance exercise, this might be achieved by varying the number of exercises and prescribing a range of sets and repetitions. For endurance training, distance prescriptions (volume) are common, with pace (intensity) the variable.

These approaches undoubtedly work; however they require a lot of trial and error to optimize, and more importantly for pain management, can be easy to overdo. Another approach, that is more self-regulating, is to control the period of time prescribed and use RPE to guide intensity. For example, using endurance exercise, such as stationary cycling on an

ergometer, if 15 min at an RPE of 7 (out of 20) is prescribed, then the pace/RPM and resistance is adjusted by the individual throughout to maintain that 7. Thus, the total volume is controlled. Time-based approaches work for all three easily scalable categories of exercise [97].

Making progress

The benefits of exercise come, in large part, to homeostatic adaptation following an imposed stressor. When it comes to pain management, improving physical qualities, such as strength, endurance and flexibility are poorly correlated with improvements in pain. Thus, the need to progress is less about direct pain management, and more about functional improvements, and possibly reduction of recurrence risk. One consideration that is often overlooked: demonstrated progress has a positive psychological effect. This can be helpful when changes to pain and function may be lagging indicators. Progress for the chronic pain patient should be structured, but flexible. Small increments, such as 5% in total weekly volume are supported by empirical evidence.

Section summary

Exercise is a biopsychosocial intervention for pain and should be implemented in such a manner. Considerations should be made for the unique status of each individual, including their beliefs and preferences, and advice and programming adapted accordingly. To ensure long-term success, an interactive/collaborative approach between practitioner and patient is optimal. This involves goal setting, along with mapping out the skills required to achieve the goal, and the behaviors needed to develop the skills. Once these skills and behaviors are mapped out, an exercise program can follow, which should ideally be optimized around the individual's current abilities, with consideration of their broader psycho-social environment. Additionally, appropriate dosage and progression will enhance the likelihood of success and minimize the chance of adverse effects.

Conclusion

With both the incidence and prevalence of chronic pain so high and the costs (both direct and indirect) so high, cost-effective and accessible interventions form a crucial aspect of effective long-term management. Chronic pain involves multiple body systems and has a big impact on psychological and social well-being as well. There are distinct neurobiological changes that are present in people with chronic pain, and there is sound mechanistic reasoning for the use of exercise to address some of these. We know that exercise is not a comprehensive solution for chronic pain, but it is a low-cost, highly accessible intervention that provides a multitude of positive secondary effects on health, in addition to the primary effects on chronic pain.

In a clinical setting, exercise is best delivered as part of an overall multi-modal treatment plan, with a multi-disciplinary team, within a framework of pain neurobiological education. The challenges faced by clinicians and patients alike pertaining to the use of exercise for chronic pain related to behavioral barriers to the beginning and continuing an exercise program, knowledge of each party, access to equipment and a safe and secure environment in which to exercise, a paucity of literature on what types of exercise, if any, are best for certain pain presentations or individuals, and the inherent difficulties in dosage and progression of exercise in a chronically sensitized individual who may not respond to exercise in the same manner as a healthy individual.

Future considerations for clinicians, researchers, and health policy relating to the implementation of exercise for chronic pain include accessibility and reimbursement, short-term outcome measures, long-term sustainability/adherence, optimal types and dosage of exercise for certain pain presentations or individuals, and predictive factors, for both positive and negative responses to exercise.

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