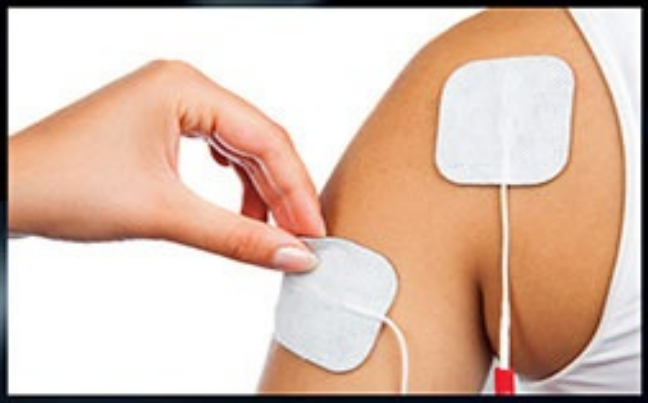
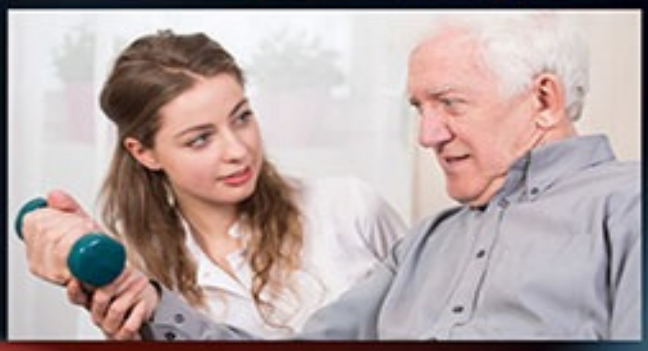
Mechanisms *and* Management *of* Pain *for the* Physical Therapist

SECOND EDITION

Kathleen A. Sluka





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Mechanisms and Management of

Pain for the Physical Therapist

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Mechanisms and Management of

Pain for the Physical Therapist

Second Edition

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FOREWORD

Pain has an element of blank;
It cannot recollect
When it began, or if there were
A day when it was not.

It has no future but itself,
Its infinite realms contain
Its past, enlightened to perceive
*New periods of pain.**

It has taken the biomedical community a very long time to begin to understand what Emily Dickinson meant when she wrote about pain in the 1800s. It is clear, however, that Kathleen Sluka and her outstanding assembly of international colleagues get it. I have been involved in teaching neuroscience and electrical modalities to physical therapy students for more than 35 years. The revolution in thinking about pain management during my time as a lecturer parallels the development of more realistic animal models of pain, incredible new techniques to explore the neural mechanisms associated with sustaining the perception of pain, a far greater understanding of personal and environmental factors that influence pain behavior, a broader array of intervention strategies based on a much more rational theoretical framework, and clinically relevant research findings. The breadth of topics in this textbook helps the reader to understand the scope of issues that fit under the umbrella of pain. After reading this text, the reader should be aware that pain, in many instances, is so much more than a single impairment in body function and structures. And it should also be clear that the effective management of pain requires an interdisciplinary approach rather than just a pill or a TENS unit. The authors skillfully argue and justify that various modalities used alone will probably not lead to clinically meaningful change in a visual analog pain scale or a sustained increase in the patient's level of activity or participation. Sluka et al. have provided a rich, evidence-based framework to understand the mechanisms for and the management of this mysterious four-letter word—pain.

Section I contains five chapters that provide an excellent and clear infrastructure for the rest of the book: identifying the relevant terms, providing clear definitions, summarizing the vast literature on putative mechanisms to describe why pain remains when the tissue is healed, and introducing the reader to the concepts of how human individual differences lead to variability in response to pain. It is fascinating to watch the story of basic science research move from the study of tail-flick behavior in the rat to indicate thermal hyperalgesia to today's sophisticated animal models in which pain is induced via a pharmacological agent or a special diet and in which mediating factors such as gender, age, and diet are examined. The behavioral studies are coupled with mechanistic studies so that insight into the spinal mechanisms is not just hypothetical; recordings from neuronal and non-neuronal cell populations, the presence of synaptic plasticity, and specific types of neuroimmune reactions are being examined in the context of pain.

Some textbooks were published on physical therapy procedures without citing a single clinical research study reference as recently as the 1970s. These earlier "how to" books did not offer guidance in selecting an intervention to match the examination findings or in selecting a particular procedure over another. If we use the earlier books as a frame of reference, the shift in physical therapy practice is dramatic. The rest of this book illustrates the shift. Section II of this text focuses attention on pain regardless of medical diagnosis, and provides guidance and evidence to support sound clinical decision making. The chapters in this section demonstrate the importance of the clinical examination, selecting the best tools to classify the pain behavior and providing help with the right tool to determine the effect of treatment outcome. Chapters on pain management in this section and Section III go beyond physical agents to provide evidence to support the use of exercise and manual therapy and to emphasize the need for interdisciplinary collaboration and the importance of including cognitive interventions. Section IV provides a series of chapters that discuss a series of pain syndromes using an evidence-based approach.

It is so exciting to see the exponential growth in research that can be used by the clinician. Mechanisms can be described that may account for the pain behavior, and evidence is available to aid in the selection of the most *effective* plan of care. We have made major strides in examining the effectiveness of particular interventions in relevant patient populations. No, we do not have the "final answers," but evidence has emerged to guide the rejection of certain modalities because studies in patients with pain do not indicate improvement with particular interventions. The interdisciplinary authors who wrote this book are conducting research at the bench or in the clinic around the world. They are

passionate about providing knowledge and skills that will be translated into clinical practice for the benefit of patients who have suffered because of our ignorance for far too long. Thank you.

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* Dickinson E. The complete poems of Emily Dickinson. Boston, MA: Little Brown; 1924. Available at www.bartelby.com/113/

PREFACE

Since the formation of the International Association for the Study of Pain (IASP) more than 40 years ago, the practice of pain management, including the role of physical therapy, has changed dramatically. Further, knowledge about the role of the peripheral and central nervous systems in processing pain signals from uninjured and injured tissue has expanded exponentially. One important recent realization is the importance of altered processing in the central nervous system, with both enhanced excitability and reduced inhibition now seen as significant contributing factors to the pain of chronic diseases. Further, the inclusion of psychosocial factors in the management of pain has greatly transformed how we approach a person with pain.

Pain severely affects function and is the main reason why people seek treatment in physical therapy. However, education about pain in physical therapy, as well as in medicine, has historically been minimal and is usually integrated into existing courses such as neuroscience, orthopedics, or physical agents. Given pain's importance in affecting an individual's function and quality of life, I believe it is important for all physical therapy students and practitioners to gain an up-to-date understanding of pain mechanisms and management. The IASP and its chapters have enhanced the understanding and treatment of pain worldwide, emphasizing an interdisciplinary approach.

A number of important events have occurred in recent years regarding pain management and education. In 2010, the IASP hosted an international summit that declared access to pain management is a fundamental human right. In 2011, the Institute of Medicine in the United States produced a blueprint for action for transforming prevention, care, education, and research to improve relief for people with pain. This, along with initiatives from the IASP, has resulted in the development of National Pain Strategies within individual countries to further transform the management of pain. In pain education, the IASP, in 2012, completely revised its curriculum guidelines for pain education for all health professionals, including physical therapy. And in 2013, an interprofessional group developed core competencies for entry-level pain education. These initiatives and the advances in research since the first publication of this book have led to the revised book.

I have developed and currently teach a stand-alone course to entry-level physical therapy students on pain mechanisms and management. This course emphasizes the latest knowledge on pain mechanisms and promotes an evidence-based and multidisciplinary approach to the management of both acute and chronic pain. This book parallels and continues to emphasize these concepts. I believe it is important to understand the mechanisms underlying pain conditions in order to better understand appropriate treatment strategies. I propose that there are essentially three potential categories into which a pain condition can fall. One group has a strong peripheral component that drives central excitability and pain. In this group, when the peripheral generator of pain is removed, the pain goes away. Acute pain syndromes commonly fall into this category. The second group has a strong central component that is independent of a peripheral pain generator. There may have been an initial peripheral pain generator, but it is no longer present, and the pain is maintained by enhanced central excitability. In this case, treatment must focus on techniques that enhance central inhibition and decrease central excitation. This category includes chronic pain conditions such as nonspecific low back pain, fibromyalgia, and temporomandibular joint disorder. The third group entails a combination of both peripheral and central sensitization so that both sites must be adequately treated in order to relieve the pain. This third group probably involves subacute as well as some chronic pain conditions. All of these conditions, whether acute or chronic, have the capacity to be modulated by psychosocial factors.

This book has been organized into four sections. The first discusses important issues in pain terminology, epidemiology, and basic science mechanisms and emphasizes the heterogeneity of pain. Importantly, this section attempts to integrate pain assessment results with basic underlying mechanisms. It further emphasizes the importance of individual pain variability by discussing differences associated with sex, gender, and age, as well as genetic determinants of variability. The second section discusses the physical therapy management of pain. We include chapters on each treatment area—education, exercise, electrical stimulation, physical agents, and manual therapy—in the management of pain. Each chapter discusses the evidence for the basic science mechanisms underlying how the treatments reduce pain, as well as the clinical evidence to support their use in patients. The third section emphasizes an interdisciplinary approach to pain, with chapters discussing the physical therapist’s role in interdisciplinary pain management, and chapters on medical and psychological management of pain. The last section includes chapters on common syndromes including myofascial pain, fibromyalgia, spinal pain, migraine, temporomandibular disorder, osteoarthritis and rheumatoid arthritis, neuropathic

pain, complex regional pain syndrome, and pain from neurological disorders. Each of these chapters describes the pathophysiology of the disease, as well as an evidence-based approach to medical management, psychological management, and physical therapy management. The final chapter of the book gives 10 case studies with explanations of the physical therapy treatment and the evidence to support that treatment. I felt it was important for this book to emphasize an evidence-based approach to the management of pain. The second edition of this book has added a number of new chapters that reflect advances in our understanding and treatment of pain. These chapters include motor control, nonspecific effects of treatment, self-management and pain, neck pain, and pain in neurological disorders.

The practice of physical therapy has changed dramatically over the last 10–15 years from one that based treatments on empirical evidence to one that bases treatments on high-quality evidence. The evidence base is incredibly important in making educated decisions in the treatment of pain. Evidence can come from strong basic science studies, experimental pain studies, and randomized controlled trials. Systematic reviews and meta-analysis combine the data from randomized controlled trials to come up with a recommendation for the use of a particular treatment in a specific condition. If there is strong evidence from systematic reviews and meta-analysis, the treatment should be used in these patients. If the primary evidence is weak or inconclusive, however, the conclusions of reviewers should be interpreted with caution because the evidence is only as good as the randomized controlled trials on which the review was based, Since the first edition of the book, there has been a substantial body of literature published on both mechanisms and clinical effectiveness of a variety of treatments. When teaching my course to physical therapy students each year, I found myself not only regularly updating all the literature in the current book but essentially replacing that literature with newer more up-to-date work, and realized a large body of evidence has been generated in just a short period of time. This growth in evidence shows the escalation of research in physical therapy and rehabilitation, and in pain management itself. This research is vitally important to the physical therapy community in terms of acceptance of techniques used in the profession, reimbursement for treatments, and the clinician’s ability to make informed decisions in the management of pain.

This book was designed to fill a gap in the education of physical therapists by supporting a more comprehensive education in the management of pain. It is designed not only to be used by students, but to be a primer for practicing physical therapists actively involved in the treatment of pain. The book will also be useful in helping other professionals involved in rehabilitation to gain a better

understanding of an evidence-based approach to the management of pain. I hope this book fills a need for physical therapy students, educators, and practitioners with an interest in an improved understanding of pain mechanisms and management.

I would like to thank the many people who made this book possible, particularly the chapter authors and coauthors who gave up their precious time to write a chapter in this book. I thank all my laboratory members who kept the experiments running while I disappeared to finalize this second edition. I thank the staff in the Department of Physical Therapy and Rehabilitation Science who diligently kept everything running behind the scenes. I also thank my husband who kept things going at home allowing me to concentrate on the revision of this book. I am also grateful for the opportunity from the IASP Press to develop this second edition to the book, and to IASP and Wolters Kluwer, particularly Nicole Dernoski, for their amazing dedication and assistance in the editing and designing of this book. I hope this book will lead to a better understanding and improved treatment of pain by physical therapists and rehabilitation professionals worldwide so that patients can get the pain relief they desperately seek.

Kathleen A. Sluka, PT, PhD, FAPTA

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SECTION 1

Basic Concepts and Mechanisms

CHAPTER 1

Introduction: Definitions, Concepts, and Models of Pain

Kathleen A. Sluka

Pain is a complex experience that is uniqcomplex experience that is unique to each individualue to each individual. As such, the experience of pain is difficult to both define and treat. Pain can arise as a result of damage to any tissue that is innervated by nociceptors, or can occur in the absence of tissue damage. For a clinician, the treatment of pain, particularly chronic pain, is difficult and unique to each patient. Everyone has or will experience pain at some point in their life. The impact of this pain may spread well beyond the perception of pain. For example, one may not be able to go to work, attend a significant family function, or participate in social activities because of the pain. Pain is now considered the "fifth vital sign," along with the measurement of blood pressure, temperature, heart rate, and respiratory rate. Further, the Joint Commission mandates that effective pain management is appropriate for all patients.

The International Association for the Study of Pain (IASP) was founded in 1973, under the impetus of John Bonica, to bring together clinicians and researchers in an attempt to improve the treatment of pain. From its beginnings, the IASP was multidisciplinary and international. IASP has nearly 7000 members from more than 100 countries, many of which have national chapters affiliated with IASP. As such, the IASP is the leading professional organization for science, practice, and education in the field of pain. Membership of IASP is open to all professionals involved in pain research or the diagnosis and treatment of pain. The association holds a biennial World Congress on Pain that is international and multidisciplinary, and publishes the leading journal in pain research, *PAIN*. Importantly, the IASP and its chapters have made a huge impact on the understanding of pain, pain education, and pain management worldwide. Guidelines for education are available for all disciplines, including medicine, nursing, psychology, and physical therapy, as well as interprofessional education.

These guidelines, updated in 2012, along with recently published pain competencies for entry-level education [4,11,17], will be the basis for the information presented in this book. These competencies represent the expectation of minimal capabilities for graduating health students for pain management. The competencies and IASP guidelines focus around four domains: multidimensional nature of pain, pain assessment and measurement, management of pain, and clinical conditions or context of pain. This book is therefore divided into sections to address these domains and includes basic concepts of pain, physical therapy management of pain, interdisciplinary management of pain, and pain syndromes.

EPIDEMIOLOGY OF PAIN

Pain is the number one reason that a person seeks medical attention, whether acute or chronic. As such, it should be addressed, and everyone has a right to pain relief. These principles were outlined in the Declaration of Montreal [16] and highlighted in the Institute of Medicine Report on Pain by the National Academy of Sciences in 2011 [9]. One hundred million adults in America suffer from chronic pain. This is greater than the number of individuals affected by diabetes, cancer, and heart disease combined [9,12]. Prevalence estimates for pain severity are 10% for moderate pain and 11% for severe pain [12].

A large-scale survey (35,718 respondents) of the U.S. population shows that 30% of the U.S. population has chronic pain lasting at least 6 months [18]; incidence is similar between White, African American, and Hispanic subjects [32] and in different populations worldwide [6,7,29,30,38]. Lower socioeconomic status, lower education, and unemployment are associated with higher prevalence of pain [18,32]. However, race and ethnicity do not predict disabling pain when socioeconomic and education characteristics were controlled [32]. A survey of chronic pain sufferers in the United States by the American Pain Foundation in 2006 shows that pain has a significant effect on everyday activities, interfering with recreational activities, household chores, and work (40–60%) [1]. For those suffering with chronic pain, participation in recreational activities is greatly limited (85%) and much greater than that for acute pain sufferers (59%) [1]. Similarly, for activities of daily living surveyed (running errands, performing household chores, taking care of self and others, traveling, and attending a public event), chronic pain sufferers had greater limitations than those with acute pain [1]. It should be emphasized, however, that

30–60% of respondents with acute pain have significant limitations in their activities of daily living as a result of the pain [1]. Interestingly, only 25% of respondents consulted a physical therapist or performed exercises (45% chronic pain; 14% acute pain) [1]. The incidence of pain is highest for low back pain (28%), but there is also a significant percentage of the population suffering from neck pain (15%), migraine (15%), and peripheral joint pain (30%; knee, 18%; shoulder, 9%) [31]. Gaskin and Richard [12] showed that the prevalence of joint pain was 33%, arthritis was 25%, and functional disability was 12%. Thus, both acute and chronic pain are common and can significantly impact quality of life by interfering with social and work activities. Chronic pain management is costly. Health care expenditures are greater with greater pain severity and for those with functional disability [12]. In the United States, pain costs over 600 billion dollars/year in health care costs and lost wages [9], and creates major human and economic costs for patients, families, and society [11]. Those with the most severe pain and functional disability have the highest health care costs and the largest impact on productivity (number of days missed, number of hours worked annually, hourly wages) [12].

Women, in general, have a higher incidence of pain than do men, particularly musculoskeletal pain, and women are more likely to have widespread pain than do men [3,13,18,19]. Pain incidence varies across the life span, with older adults showing a greater incidence of pain than young adults [18]. For example, 15% of women of the 18-to-24-year age group had chronic pain, whereas 42% of those 65 and older had chronic pain.

Incidence in children of chronic pain varies between 5% and 50%, with weekly headaches occurring in 23%, back pain reported in up to 20%, migraines in 8%, and 15% with pain two to three times per week [21]. Higher rates occur more commonly in girls and in those with lower socioeconomic status [21]. In community-dwelling older adults, nearly 50% seek treatment for daily pain, and 50–85% of nursing home residents experience pain [15,38]. Further, nearly 50% of nursing home residents with pain do not receive adequate pain management, and those numbers are greater for those with dementia or non-White residents [15,34,40]. Pain in children, in older adults, and those with cognitive impairments is frequently undertreated [5,10]. For example, cognitively impaired older adults with hip fractures are less likely to receive adequate pain medication than those who can verbally express their pain [28]. Undertreatment of pain has many potential detrimental consequences that affect the individual and the family. These include increased psychological distress, malnutrition, impaired sleep, impaired function, declined socialization and recreational activities, and reduced quality of life [8,15]. Thus, recognition that pain varies on

the basis of multiple factors including sex, race, age, and socioeconomic status is essential to providing adequate pain management.

PAIN DEFINITIONS

The IASP defines pain as an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage (www.iasp-pain.org). Inherent in this definition is the underlying premise that pain does not have to be associated with observable tissue damage or have a detectable underlying cause. Pain is multidimensional, involving not only the sensation of pain but also the emotional experience associated with pain. Importantly, pain is subjective and, if described by the patient, is real.

Melzack and Casey [26] propose three dimensions of pain: the sensory discriminative, motivational affective, and the cognitive evaluative (Fig. 1-1). The sensory discriminative dimension of pain refers to the sensation of pain and includes the location, quality (e.g., burning, dull, sharp), intensity, and duration. The motivational affective dimension refers to the unpleasantness of pain or how much the pain bothers the patient (e.g., nauseating, sickening). The cognitive evaluative dimension puts pain in terms of past experiences and probability of outcome and can as such modify both the sensory discriminative and the motivational affective dimensions. This cognitive dimension can thus negatively or positively affect the outcome and is based on the patient's beliefs. These beliefs include culture, past experiences, and prior experiences by themselves or others. For example, if a person experiences low back pain for the second time, he or she may be more likely to do well treatment during the first experience resolved pain quickly. On the other hand, if a person with low back pain has had multiple episodes of pain that were not adequately treated or resolved in prior occurrences, the pain may be more difficult to treat. All three dimensions are linked and interact to affect the motor and behavioral consequences responsible for the complex pattern of responses to pain.

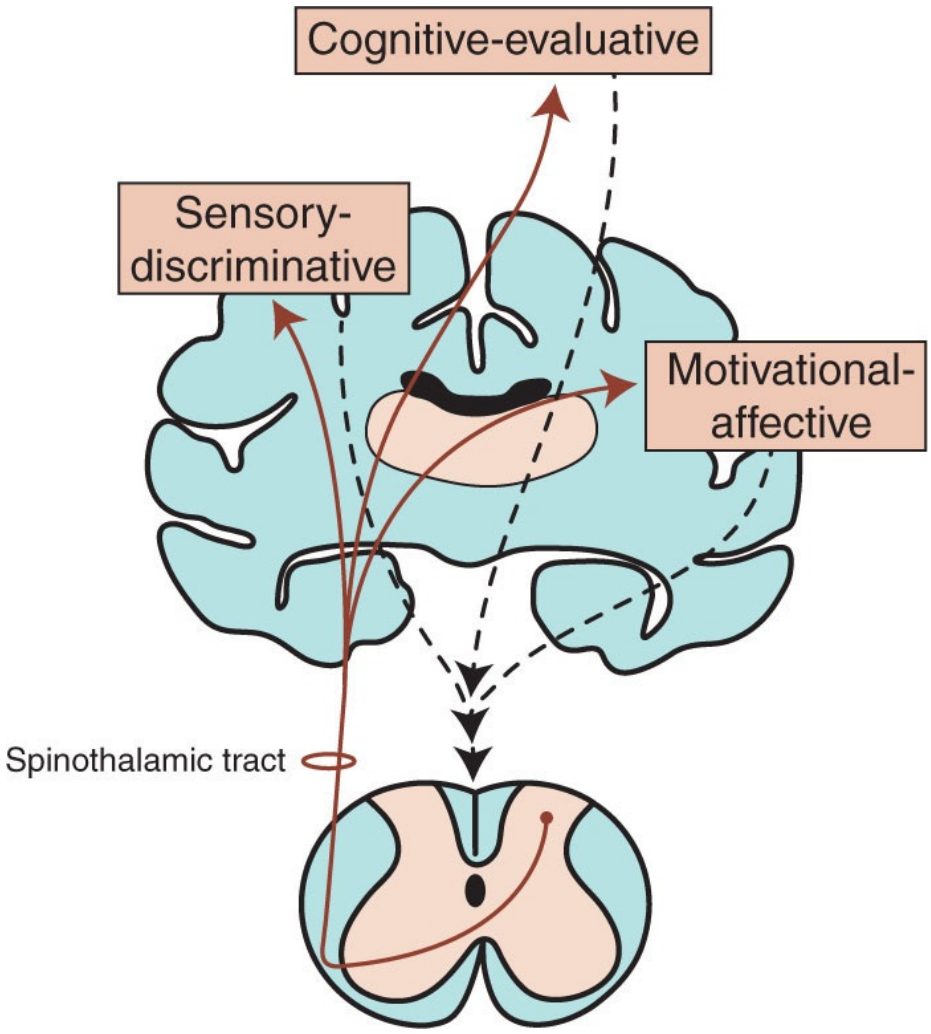

FIGURE 1-1 The dimensions of pain as outlined by Melzack and Casey in 1968.

IASP has formulated other definitions that are useful for describing pain (www.iasp-pain.org) (Table 1-1). Hyperalgesia is an increased sensitivity to a noxious stimulus and can occur both at the site of injury, primary hyperalgesia, and outside the site of injury, secondary hyperalgesia. Hyperalgesia may include both a decrease in threshold and an increase in suprathreshold response. Allodynia is a term used to describe pain from a nonnociceptive stimulus. Thus, brushing the skin after a sunburn could be considered allodynia, whereas pressure applied to an inflamed joint could be considered hyperalgesia. Basic research suggests that the underlying neural mechanisms for primary hyperalgesia involve increased responsiveness of nociceptors (see Chapter 2). On the other hand, the underlying mechanisms of secondary hyperalgesia and allodynia appear to involve increased responsiveness of central neurons (see Chapter 3). Referred pain, common in both acute and chronic pain conditions, is

spontaneous pain perceived outside the area of injury. It usually, but not always, follows a dermatome or spinal segmental area. However, it can be referred to areas quite distant from the site of injury. The most common example of referred pain is pain that radiates down the arm during a heart attack. Table 1-1 lists other terminology useful to the assessment and understanding of pain.

TABLE 1-1 Pain Terminology

Pain	An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms as such
Hyperalgesia	Increased pain sensitivity
Allodynia	Painful response to a nonnociceptive stimulus
Hypoalgesia	Absence of pain in response to stimulation that would normally be painful
Dysesthesia	An unpleasant abnormal sensation, whether spontaneous or evoked
Neurogenic pain	Pain initiated or caused by a primary lesion, dysfunction, or transitory perturbation in the peripheral or central nervous system
Neuropathic pain	Pain arising as a direct consequence of a lesion or disease affecting the somatosensory system
Pain threshold	The least experience of pain that a subject can recognize
Pain tolerance	The greatest level of pain that a subject is prepared to tolerate
Pain behavior	A pattern of audible or observable actions, posture, facial expressions, verbalizations
Referred pain	Spontaneous pain outside the area of injury
Noxious stimulus	An actually or potentially tissue-damaging stimulus
Nociceptor	A sensory receptor that is capable of transducing and encoding a noxious stimulus
Nociceptive neuron	A central or peripheral neuron that is capable of encoding noxious stimulation
Nociception	The neural process of encoding and processing noxious stimuli
Nociceptive pain	Pain arising from activation of nociceptors
Sensitization	Increased responsiveness of neurons to their normal input or recruitment of a response to normally subthreshold inputs
Peripheral sensitization	Increased responsiveness and reduced threshold of nociceptors to stimulation of their receptive fields
Central sensitization	Increased responsiveness of nociceptive neurons in the central nervous system to their normal or subthreshold afferent input

Source: From www.iasp-pain.org

ACUTE AND CHRONIC PAIN

Pain can be referred to as either acute pain or chronic pain. Distinct differences exist between these two pain conditions that should be recognized. Specifically, acute pain occurs as a direct result of tissue damage or potential tissue damage, and is a symptom. As such, it has a well-defined time of onset with clear

pathology. Acute pain serves to protect from tissue damage, and if tissue damage has occurred, to allow time for healing. Acute pain that requires clinical treatment usually results from observable tissue damage, including injury, surgery, or procedures such as wound debridement. Acute pain can be adequately treated with pharmacological and nonpharmacological treatments aimed at the peripheral tissue damage. For example, nonsteroidal anti-inflammatory drugs or ice are commonly utilized for treatment of acute inflammation associated with ankle sprain. Thus, acute pain serves a useful and protective function.

Chronic pain, on the other hand, is not protective and does not serve a biological purpose. Pain can be considered chronic if it (1) outlasts normal tissue healing time, (2) the impairment is greater than would be expected from the physical findings or injury, and/or (3) pain occurs in the absence of identifiable tissue damage. In addition, many clinicians define chronic pain in terms of the number of months after the initial injury, usually 3–6 months after injury. The use of a time frame to diagnose chronicity of pain is useful for some conditions such as osteoarthritis. It is not useful, however, for other conditions that may take a long time to heal, for conditions that were not adequately treated at the time of onset such that healing did not occur, or an athlete who constantly reinjures a joint because he or she does not wait for an adequate amount of time for healing to occur. Although most acute pain cases resolve within 3 months, the remaining cases that are now considered chronic cost billions of dollars per year in health care and lost wages. Thus, when pain becomes chronic, it is no longer a symptom, but is considered the disease itself. Chronic pain is difficult to treat and responds best to an interdisciplinary approach.

CUTANEOUS VERSUS DEEP-TISSUE PAIN

Pain from deep somatic and visceral tissues is uniquely different from cutaneous pain. Cutaneous pain is generally easy to locate, sharp, and does not usually refer. On the other hand, deep-tissue pain from muscle, joint, or viscera can be difficult to locate, diffuse, and routinely refers to other structures at times quite distant from the site of injury [20,23,35]. For example, visceral pain is often referred to muscle and cutaneous structures. In fact, people with visceral pain conditions such as irritable bowel syndrome show development of referred pain and muscle hyperalgesia [14]. Similarly, people with somatic deep-tissue pain, such as osteoarthritis or myofascial pain, also develop referred pain and muscle

hyperalgesia at sites outside the site of injury [14]. For muscle pain, the size of the area of referred pain correlates with the intensity and duration of the primary muscle pain [35]. In human subjects, painful intramuscular stimulation is rated as more unpleasant than painful cutaneous stimulation [36], pain is longer lasting, and referred pain is more frequent [39]. Thus, differentiation of primary and secondary hyperalgesia is critical to accurately treat patients with pain. This may prove difficult in some patients who show tenderness and increased muscle activity, as well as visceral or deep somatic pain.

PAIN THEORIES

Specificity Theory

Initial theories attempted to describe all sensory experiences, that is, touch, heat, cold, and pain, using one theory. These included the specificity theory and the pattern theory with evidence to support the specificity theory for most sensations. However, both theories were inadequate to describe the sensation of pain. The *specificity theory* suggests that there are separate nerve endings for each variety of sensation arising from cutaneous stimulation, that is, touch, cold, warmth, and pain. For pain, the theory suggests that there are “pain receptors” that when stimulated always produce the sensation of pain and only pain. However, for pain, this theory cannot fully explain certain phenomena experienced by a painful stimulus or certain pain conditions. For example, phantom limb pain persists in the absence of the nociceptor, lesions of the central pain pathways do not completely abolish pain, and pain can return following the lesion. Furthermore, touch can elicit pain, that is, allodynia, and pain can continue after removal of the noxious stimulus.

Pattern Theory

The *pattern theory* suggests that pain would result from a patterned input from sense organs in the skin (spatial and temporal impulses in the central nervous system [CNS]). Sensation is thus a learning event that does not require a specific sensory channel. However, it is clear that there are specialized sensory endings that respond to noxious stimuli and there are central pathways that transmit pain sensation, that is, spinothalamic tract.

Gate Control Theory of Pain

In 1965, more than 40 years ago, Melzack and Wall [27] proposed the *gate control theory of pain*, which utilized concepts from both the specificity theory and the pattern theory. This theory is an integrative model that took into account both the physiological and the psychological components of pain. The gate control theory of pain profoundly influenced the study of pain and was the stimulus for the development of new pain treatments. The theory suggests that there are specialized nerve endings, nociceptors, whose response is modulated in the dorsal horn of the spinal cord (Fig. 1-2). Input from large-diameter afferents (nonnociceptors) and small-diameter afferents (nociceptors) are "gated" in the spinal cord. These two inputs converge on a substantia gelatinosa (SG) neuron in the dorsal horn of the spinal cord, as well as a T cell. The SG neuron is inhibitory to the T cell that initiates the consequences of pain, that is, motor, sensory, and autonomic responses. The theory suggests that there is a balance between large- and small-diameter afferent input that under normal conditions favors an inhibition of the system and thus there is no pain experienced. Input from nociceptors inhibits the SG neuron, allowing the T cell to fire, "opening the gate," and thus results in pain. The theory further suggests that increasing input from large-diameter input results in a "closing of the gate" by increasing firing of the SG neuron to inhibit nociceptor activity and subsequently decreasing firing of the T cell to result in a reduction in pain. In addition, the theory proposes that this system is under the control of supraspinal sites that could further modulate pain. This theory was used to explain sensory phenomena unique to pain such as the fact that stimulation of a single nociceptor does not always elicit pain, repetitive noxious stimulation results in increasing pain, and large-fiber input inhibits pain. It was also used to explain clinical pain conditions such as phantom limb pain and causalgia.

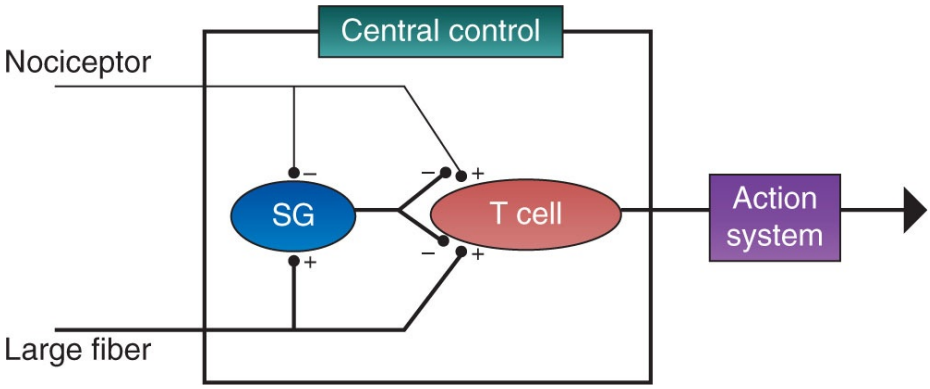

FIGURE 1-2 The gate control theory of pain as initially described by Melzack

and Wall in 1965. SG, substantia gelatinosa neuron in the spinal cord; T cell, transmission cell that activates the action system or the response to pain; ‘+’, excitatory synapse; ‘−’, inhibitory synapse. (Figure redrawn from [27].)

Many criticize the theory, however, stating it as an oversimplification and that several of the tenets in the original theory have not held up over the past 40 years. For example, the theory suggests that nociceptors are tonically active. Subsequently, neurophysiological studies show that nociceptors are not spontaneously active but rather fire in response to a noxiously applied stimulus in uninjured tissue. The theory also suggests that nociceptors are directly inhibitory to the SG cell, but again, this has not held true, and nociceptors are indeed excitatory. The theory further proposes that neurons respond to both noxious and innocuous stimuli. However, subsequent studies show there are also neurons in the SG that respond only to noxious stimuli and do not receive input from large-diameter afferent fibers. The theory also relied heavily on the concept of presynaptic inhibition, for which there is strong evidence. Since the time the theory was proposed, it has also become clear that there are postsynaptic mechanisms responsible for inhibition in the spinal cord as well. Furthermore, since the original theory was proposed, there is substantial evidence (see Chapters 2 and 3) that the central control system (supraspinal sites) both facilitates and inhibits pain at the level of the spinal cord. Regardless of these details, the idea of a central control and modulation of pain remains and is used to explain a variety of pain conditions and treatments. Treatments such as transcutaneous electrical nerve stimulation (TENS) were initially designed on the basis of the gate control theory to increase large-diameter input to the spinal cord to inhibit pain. Subsequent research has shown that TENS additionally utilizes supraspinal control sites to inhibit activity of dorsal horn neurons in the spinal cord. Thus, the idea of the gate control theory of pain generated a substantial amount of research that has advanced the field tremendously in the last 50-plus years. It has resulted in the recognition that pain is a CNS phenomenon, that treatments for pain must be aimed not only at the peripheral nervous system but also at modulating the CNS, and that pain is multidimensional.

Neuromatrix Theory

The neuromatrix theory has evolved from the gate control theory of pain and was first described and published by Melzack in 1991 [24,25]. This theory proposes a large, widespread network of neurons that integrates the thalamus,

cortex, and limbic system that is initially genetically determined and later sculpted by external (sensory) inputs, termed the body-self. This network imparts a characteristic pattern or output, termed the neurosignature, that is projected to areas of the brain for awareness of pain, and motor output or movement. The neurosignature pattern is modulated by sensory inputs and cognitive events, and as such is a plastic system that results in an individualized response to a noxious stimulus. It is important to understand that pain is processed in the brain at the cortical level where awareness of the sensation occurs. However, pain often occurs following activation of nociceptors, can be maintained by continued nociceptor activation, and is modified by spinal and subcortical brainstem structures. Further, other systems can influence nociceptor and central nociceptive neuron activity, including nonneuronal cells such as local and circulating immune cells, hormones such as cortisol or estradiol, and factors released from muscle fibers such as adenosine triphosphate (ATP) or lactate. Fig. 1-3 depicts the original neuromatrix theory showing the body-self in the center and comprises the sensory (S), affective (A), and cognitive (C) components. This body-self neuromatrix is influenced by multiple systems, including input from nociceptors directly, cortical sites involved in cognitive and evaluative function, and systemic systems. The outputs of the neuromatrix are multiple and focus around perception of pain, direct actions in response to pain, or stress-related responses to pain. Together, these data represent a complex network of systems that interact to modify and influence the perception and response to noxious stimuli, and further explain how pain could persist in the absence of noxious stimuli. As will become apparent in Chapter 3, multiple potential sites with the cortex, as well as the brainstem and spinal cord, modulate and integrate noxious stimuli to result in a perception of and response to pain.

TREATMENT MODELS

Biomedical Model

Using *a biomedical model* to treat pain assumes that all pain has a distinct physiological cause and clinicians should be able to find and treat that physiological problem. Indeed, for treatment of acute pain, the biomedical model is appropriate and necessary. For example, for a person with a sprained ankle, treatment with adequate medical management, that is, pharmacology, bracing, physical therapy, and techniques to promote healing, resolves the pain. In this

case, pain is considered a symptom of the initial injury, and the treatments are geared to treating the injury. However, for the treatment of chronic pain, the biomedical model is inadequate.

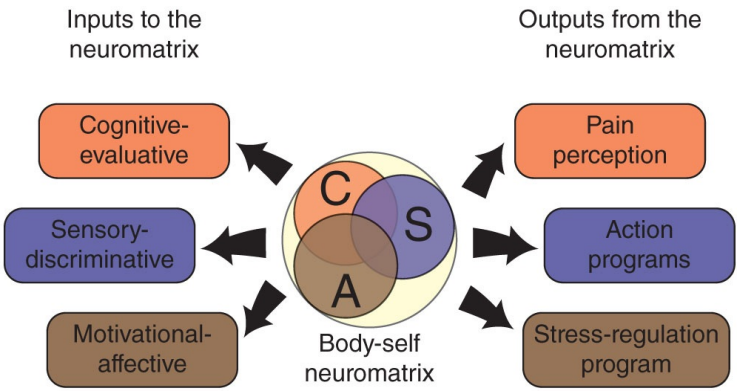

FIGURE 1-3 Schematic drawing of the neuromatrix outlined in [24].

Biopsychosocial Model

The *biopsychosocial model* is an alternative approach to the biomedical model and is particularly useful for the treatment of chronic pain. The biopsychosocial model views pain as an interaction between the biological, psychological, and sociocultural variables. The biopsychosocial model has been described in a variety of ways by a number of investigators. A schematic diagram is often drawn to represent the different aspects of the pain experience (see Fig. 1-4). In all variants of the model, nociception is the first component and represents the detection of tissue damage and activation of nociceptors and the nociceptive pathway in the CNS. The second component is pain and involves recognition of pain at the cortical level as a consequence of nociception. It is important to recognize that pain does not occur until the signal reaches the cortex and perception of pain is recognized by the patient. From here, the psychosocial aspects of pain come into play. Loeser's model [22] suggests the next component to be suffering, a state of emotional distress associated with events that threaten the biological and/or psychosocial integrity of the individual. Suffering is the negative affective response brought about by pain, such as depression, anxiety, or fear. Suffering often accompanies severe pain, but can occur in its absence. It should be clear that pain and suffering are distinct phenomena. The fourth component is pain behavior or the outward manifestation of the pain event. Pain behaviors are influenced by cultural background and environmental factors, and include both verbal and nonverbal behaviors. Examples of pain behaviors include simple facial expressions, but may also include complex behavior such

as not returning to work or avoidance of physical activity, that is, fear avoidance. The avoidance of activity stems from a fear of reinjury or harm and is particularly problematic for physical therapists to engage patients in an active treatment program. Turk has added a component (or replaced suffering), pain appraisal, which refers to the meaning that is attributed to the pain experience [37]. As an example, a person with pain may choose to continue working and socializing or may avoid all activity and work. Social roles or environment factors that take into account how the pain affects the person's role in society has also been added [37]. All of these factors together represent the biopsychosocial model that must be addressed to adequately resolve issues associated with chronic pain. Further, in acute pain, psychosocial factors affect the severity of the pain and response to treatment and can influence the transition from acute to chronic pain. For example, people with high pain catastrophizing, a set of negative cognitive and emotional schema, is a predictor of poor outcome in those with both acute and chronic pain and a significant factor in the development of chronic pain after a postoperative procedure [33]. All biopsychosocial factors will not be present in all persons with pain, but likely multiple factors will be responsible for the pain experience in an individual. Further, these factors vary across time within a patient's life and are modifiable by the external environment. For example, an anterior cruciate ligament tear will likely result in significantly more suffering and illness behavior for the professional basketball player than for the computer programmer, who may not suffer. Alternatively, the impact of a simple fall may cause more fear and concern in an 80-year-old adult with osteoporosis than when that same person was a 20-year-old, active college student.

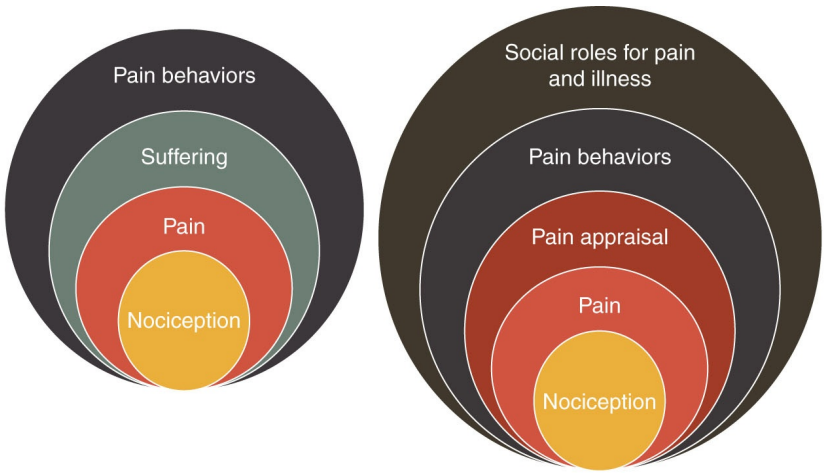

FIGURE 1-4 Schematic diagram showing the biopsychosocial model of pain as conceived by Loeser [22].

International Classification of Functioning, Disability, and Health Model

The World Health Organization published the International Classification of Functioning, Disability, and Health (ICF) in 2001 [21]. ICF is a classification of human functioning and disability. The goal of the ICF is to provide a unified and standard language for the description of health and health-related components of well-being, and the domains are therefore health and health-related ones. There are two basic lists, namely, (1) body function and structures and (2) activities and participation. Functioning encompasses body functions, activities, and participation, while disability encompasses impairments, activity limitations, and participation restrictions. Health conditions are classified with the ICD-10 (International Classification of Diseases, Tenth Revision), while functioning and disability are classified with the ICF. The ICD-10 provides a diagnosis of disease or health condition and should be combined with the ICF to classify the impact of the disease on functioning and disability. Therefore, the ICF when combined with the ICD-10 provides a means to diagnose a pain condition, in addition to evaluating the impact of the pain condition on the individual's function, and the disability that may result from the pain condition.

The American Physical Therapy Association (APTA) has endorsed and adopted the use of the ICF model for physical therapy practice, and describes its use in physical therapy practice in the current Guide to Physical Therapy Practice published in 2014 [2]. Fig. 1-5 shows the structure of the ICF model of functioning and disability as proposed by the APTA. It describes two major parts. Part 1 is a description of function and disability associated with a health condition, and Part 2 is a description of contextual factors including external environmental factors and internal personal factors. All of these factors are interactive, and changes in one factor could influence another factor but do not inherently result in disability.

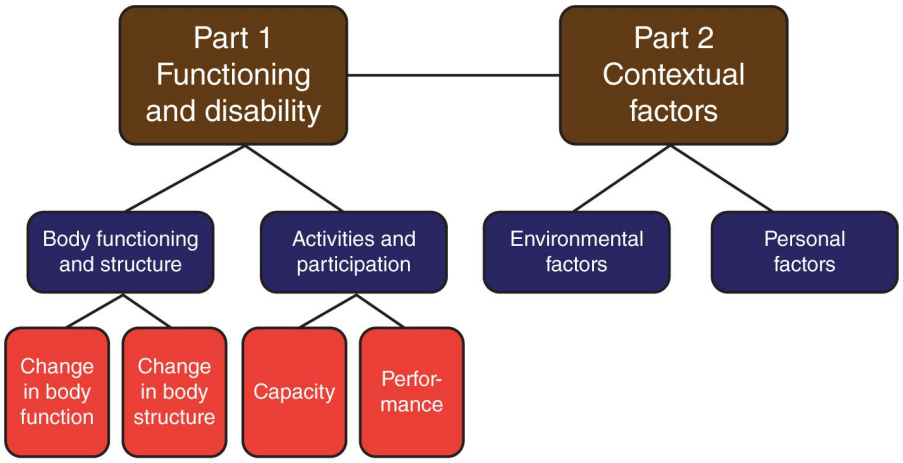

FIGURE 1-5 Schematic diagram of the ICF model as outlined in the Guide to Physical Therapy Practice [2].

PHYSICAL THERAPY PRACTICE

The practice of physical therapy is a dynamic profession aimed at restoring, maintaining, and promoting optimal physical function. Physical therapists are key providers in the health care team and work closely with other members of the team to provide an integrated approach to the plan of care. The rehabilitation approach uses multiple potential techniques, including education and self-management, exercise and physical activity, manual therapy, and electrophysical agents. For acute pain conditions associated with tissue damage and nociceptive pain, this biomedical approach to pain management may be adequate and is likely to be successful. However, it should be recognized that biopsychosocial factors influence many aspects of acute as well as chronic pain, which can predict improved or poor outcome. For example, worse outcomes are associated with (1) worse pain: higher pain intensity, longer pain duration, previous pain episodes, and multiples sites of pain, (2) higher psychological distress: fear, anxiety, pain catastrophizing, and depression, (3) lower social function: lower socioeconomic status, lower education, poor coping strategies, living alone, and less social support, and (4) general biological factors: female sex, obesity, and physical inactivity. Many of these factors are modifiable and will require an interdisciplinary approach to treatment. This is particularly true for those with chronic pain conditions, but these factors should also be addressed in acute pain conditions to avoid the patient transitioning to a chronic pain condition. If pain does become chronic, physical therapy practice should shift to enhancing the active involvement of the patient with education on activity modification, self-

management skills, and exercise, while minimizing passive treatments such as manual therapy and physical modalities. Manual therapy and physical modalities in these individuals would be utilized to enhance an active exercise-oriented approach. Further, in some patients with acute pain, the pain is not proportional to the amount of tissue damage and thus likely involves significant amounts of CNS changes and psychosocial variables that need to be addressed. In the chapters ahead, we will discuss in more detail a general approach to physical therapy treatment of pain, and examine the underlying mechanisms and clinical evidence for physical therapy treatments for pain. In addition, we will address the basic science mechanisms of pain transmission, the interdisciplinary management of pain including medical and psychological approaches, and common pain syndromes.

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CHAPTER 2

Peripheral Pathways Involved in Nociception

Kathleen A. Sluka

The peripheral nervous system plays a major role in the generation and maintenance of both acute and chronic pain. After acute injury, mediators associated with inflammation and tissue injury can directly activate nociceptors to increase inputs to the central nervous system (CNS). In more chronic conditions, continued input from nociceptors and changes in nociceptor sensitivity play a major role in maintaining the ongoing pain. For example, in people with phantom limb pain, fibromyalgia, neuropathic pain, myofascial pain, and osteoarthritis, infusion of local anesthetic into the primary pain site relieves a great portion of their pain and in some patients, completely eliminates a person's pain [2,76,181,183,195–197].

Pain is a subjective perception processed in the cortex, whereas activation of nociceptors can initiate and drive pain by transmitting nociceptive signals from the site of insult to the CNS, which eventually reach the cortex for pain perception. Further nociceptive stimuli produce a number of subcortical responses such as activation of the sympathetic system, flexion reflex, and brainstem modulation pathways. This chapter is designed to give the reader a general understanding of the characteristics of primary afferent fibers that convey nociceptive information to the CNS. It will further describe the neurotransmitters, receptors, and ion channels involved in nociception, as well as nonneuronal activators of nociceptors. Lastly, an overview of the animal models of pain that are commonly used to model clinical pain conditions will be described.

SENSORY RECEPTORS AND PATHWAYS

Cutaneous sensory receptors convey electrical signals from encapsulated, touch receptors to the CNS via Aβ fibers. Muscle spindles are mechanoreceptors that

are specialized to respond to the rate of change in muscle length or to muscle length and are carried to the CNS through Group Ia and Group II fibers, respectively. Group II primary afferents that innervate joints are large myelinated afferents that transmit information about proprioception of the joint. Other specialized nerve endings carried by large-diameter afferents from skin, muscle, and joint are listed in Table 2-1. On the other hand, **nociceptors** are unencapsulated receptors, termed free nerve endings, that respond to noxious stimuli; they include Aδ (Group III; thinly myelinated axons) and C fibers (Group IV; unmyelinated axons).

TABLE 2-1 **Peripheral Afferent Fiber Classification**

Axon Class Skin/Viscera (Muscle/ Joint)	Myelinated	Conduction Velocity (m/s)	Specialized Ending	Receptor Location	Sensation
Ia	Yes	70–120	Muscle spindle	Muscle	Proprio-ception
Ib	Yes	70–120	Golgi tendon organ	Tendon	Muscle stretch or contraction
Aβ (II)	Yes	25–70	Meissner corpuscle, Merkel cell, Pacinian corpuscle, Ruffini ending, hair follicle, paciniform endings, muscle spindle	Skin, joint, muscle	Touch, pressure, vibration, position sense, stretch of muscle
Aδ (III)	Yes (thinly myelinated)	2–25	Free nerve ending	Skin, muscle, joint, tendon, intervertebral disk, bone, periosteum, fascia	Noxious stimuli
C (IV)	No	<2	Free nerve ending	Skin, muscle, joint, tendon, intervertebral disk, bone, periosteum, fascia	Noxious stimuli

Primary afferent neurons are pseudo-unipolar neurons with a cell body located in the dorsal root ganglia (DRG), a peripheral process innervating peripheral structures, and a central process terminating in the spinal cord dorsal horn or medulla. For the limbs and trunk, the cell bodies of the sensory neurons are located in the DRG. For the head and face, the sensory neuron cell bodies are located in the trigeminal ganglia (Fig. 2-1). Primary afferent fibers vary in size and conduction velocity from thickly myelinated (Ia) to unmyelinated (C) fibers (Table 2-1).

All sensory neurons are activated by adequate stimuli. The adequate stimuli

for nociceptors reflect tissue-damaging stimuli unique to the innervated tissue, whereas for nonnociceptors, these stimuli are typically involved in sensation unique to the structure of the innervated tissue. For example, the adequate stimulus to activate a Pacinian corpuscle is vibration, whereas that for a muscle spindle is muscle length or rate of change in muscle length.

Nociceptors

A **nociceptor** is a sensory receptor that is capable of transducing and encoding actually or potentially tissue-damaging stimuli (**noxious stimuli**) (Table 2-1). Nociceptors convert mechanical, thermal, and chemical energy into electrical signals and carry this information to the CNS. The peripheral terminals of nociceptors, free nerve endings, are found in and/or around most tissues including skin, muscle, tendons, joint structures, periosteum, intervertebral disks and even within peripheral nerves (nervi nervorum) [207]. For nociceptors from different tissues, the adequate stimulus is distinctly different. For example, one of the adequate stimuli to activate a cutaneous nociceptor is cutting the skin, whereas cutting the viscera does not activate visceral nociceptors.

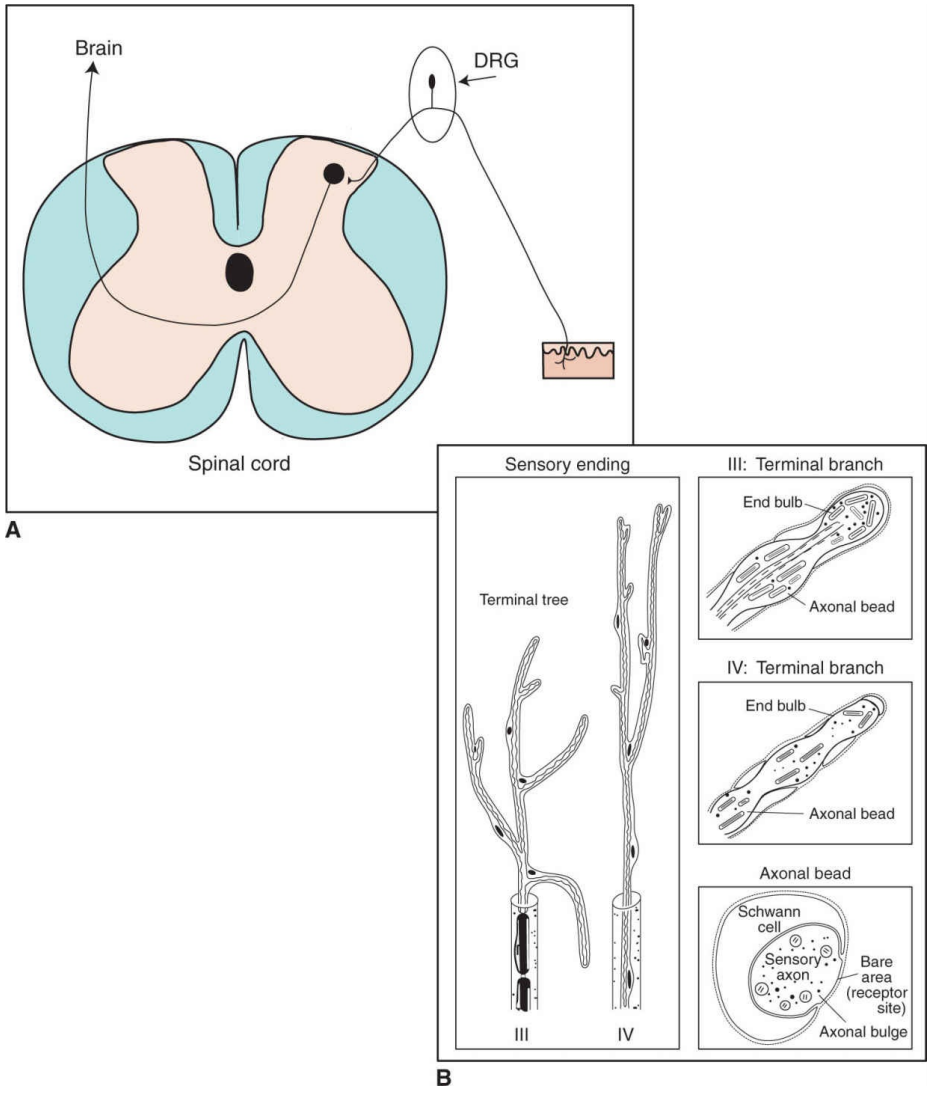

FIGURE 2-1 **A:** Schematic drawing of the nociceptor innervation of the skin, the cell body in the DRG, and the peripheral and central terminals of the nociceptor. The nociceptor synapses in the spinal cord with a spinothalamic tract neuron that transmits nociceptive information to the brain for perception of pain. **B:** Serial reconstructions of the free nerve endings of nociceptors innervating the knee joint. Terminal branches of Groups III and IV show axonal beads where they likely release neurotransmitters and contain receptors capable of transducing mechanical, thermal, and chemical stimuli. DRG, dorsal root ganglia. (Reproduced from Schmidt et al. [152] with permission of the International Association for the Study of Pain.)

Cutaneous Nociceptors

The free nerve endings of cutaneous Aδ and C nociceptors respond to noxious

mechanical and/or thermal stimuli. Many cutaneous nociceptors respond to multiple noxious stimuli including mechanical, thermal, and chemical, and hence are called *polymodal* nociceptors [145,153]. A third group of nociceptors has been identified as *silent* or mechanically insensitive and are likely activated by inflammatory mediators such as prostaglandins. The adequate stimulus to activate a cutaneous nociceptor is a noxious mechanical, heat, or cold stimulus.

Muscle and Joint Nociceptors

The primary afferent fibers innervating muscle and joint nerves are classified as Groups II, III, and IV [78,111,147,148,151,207]. Group III primary afferent fibers are thinly myelinated fibers, and Group IV are unmyelinated fibers. Both Group III and Group IV fibers transmit nociceptive information from free nerve endings in the periphery to the spinal cord dorsal horn. The adequate stimulus to activate a joint nociceptor is mechanical and usually involves stretching of the capsular tissue at end of range, or pressure applied directly over the capsule. Adequate stimuli to activate stimuli to activate a muscle nociceptor are pressure and ischemia [46,111,113].

Visceral Nociceptors

Primary afferent fibers innervating the viscera consist entirely of Aδ and C fibers [62]. Nociceptors of the viscera are considered polymodal, responding not only to mechanical stimuli, but also to heat and chemical stimuli [62]. For hollow visceral organs, the adequate stimulus to activate visceral nociceptors is distention [62]. However, 68% of visceral mechanonociceptors are activated by low-intensity distention, whereas the remaining 32% are activated by high-intensity distention.

Silent Nociceptors

Some nociceptors are normally silent, but after tissue injury, they become activated and respond to noxious stimuli. For example, Schaible and Schmidt [151] showed that before experimental knee joint inflammation, some Group III and IV nociceptors do not spontaneously fire or respond to noxious knee joint movement. After the inflammation, however, these nociceptors fire spontaneously, and now respond to noxious joint movement (Fig. 2-2). Substances released as a result of the injury may sensitize the nociceptors, allowing them to fire to lower-intensity stimuli (see section “Peripheral

Sensitization" below). Silent nociceptors were initially located in joint tissue, but have since been located in skin and viscera as well [62,149,153]. Approximately one-third of nociceptors innervating the joint, skin, or viscera are silent [62,149,153] and become activated after tissue damage.

PERIPHERAL SENSITIZATION

The sensitivity of nociceptors to painful stimuli is modifiable, increasing or decreasing in response to peripherally applied mechanical, thermal, or chemical stimuli. **Sensitization** is a term used to describe changes in nociceptive neurons after tissue injury. It is defined as an increased responsiveness of neurons to their normal input or recruitment of a response to normally subthreshold inputs (Table 2-2). **Peripheral sensitization** refers to an increased responsiveness and reduced threshold of nociceptors to stimulation of their receptive fields. Many neuronal and nonneuronal substances are capable of sensitizing primary afferent fibers and are described below.

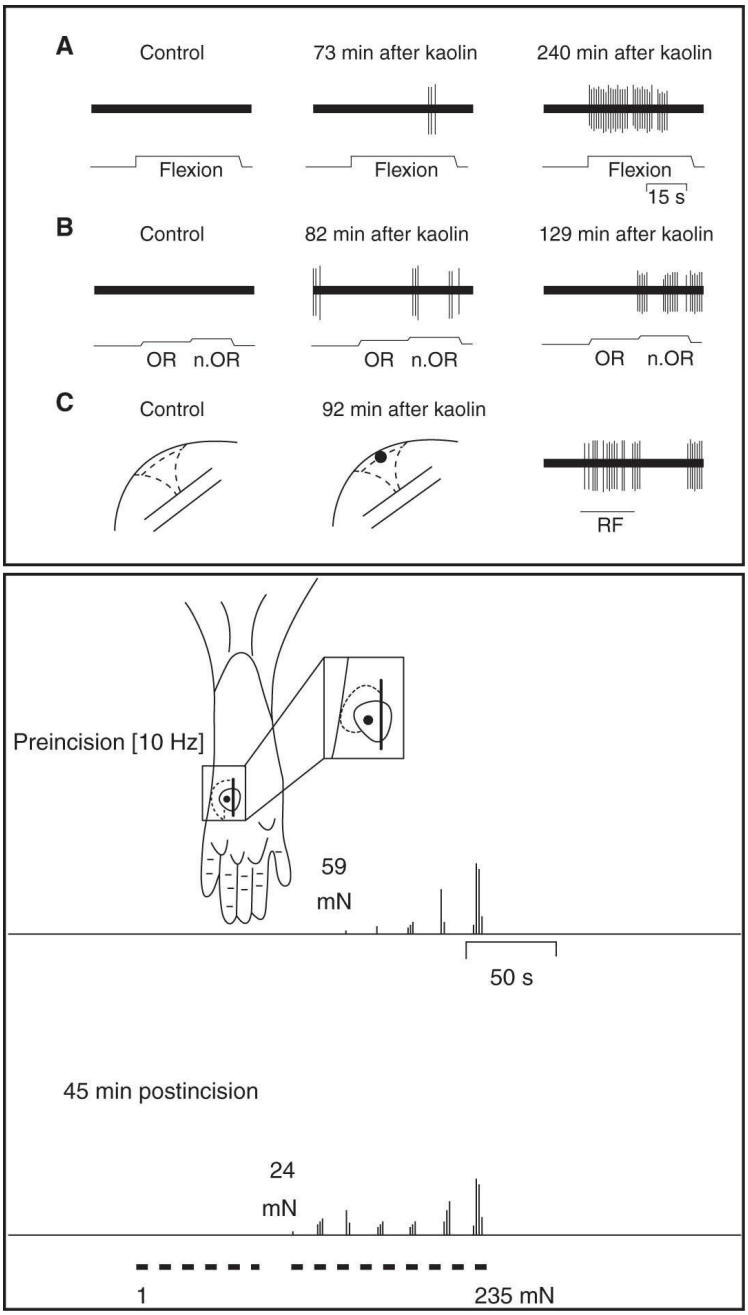

FIGURE 2-2 Sensitization of primary afferent fibers is observed by recording from isolated afferents before and after tissue injury. Top figure shows the recordings from a silent nociceptor before induction of knee joint inflammation **(A)** and for up to 4 hours after inflammation **(B)**. Development of a mechanical receptive field after inflammation **(C)**. Notice that the neuron did not respond before inflammation (kaolin/carrageenan). After inflammation, the neuron now responded to noxious and innocuous movement of the knee joint. (Reproduced from Schaible and Schmidt [150] with permission of the American Physiological Society.) Bottom figure shows recordings from a primary afferent nociceptor

before hind paw incision, and 45 minutes after incision. Responses to different forces of mechanical stimuli applied with a von Frey filament are shown. Notice that there was a decrease in threshold after injury, as well as an increase in responsiveness of the neuron to repeated stimulation. Also notice that there was a small increase in the receptive field after incision. (Reproduced from Hamalainen et al. [74] with permission of the American Physiological Society.)

TABLE 2-2 Definitions Relevant to Nociception

Noxious stimulus	An actually or potentially tissue-damaging stimulus
Nociceptor	A sensory receptor that is capable of transducing and encoding a noxious stimulus
Nociceptive neuron	A central or peripheral neuron that is capable of encoding noxious stimulation
Nociception	The neural process of encoding and processing noxious stimuli
Nociceptive pain	Pain arising from activation of nociceptors
Sensitization	Increased responsiveness of neurons to their normal input or recruitment of a response to normally subthreshold inputs
Peripheral sensitization	Increased responsiveness and reduced threshold of nociceptors to stimulation of their receptive fields
Central sensitization	Increased responsiveness of nociceptive neurons in the central nervous system to their normal or subthreshold afferent input

Source: From www.iasp-pain.org

Sensitization of a neuron is characterized by increased spontaneous activity, a decrease in threshold of response to noxious stimuli, an increase in responsiveness to the same noxious stimuli, and/or an increase in receptive field size. Recording the activity of peripheral nerves before and after induction of acute inflammation, Schaible and Schmidt [148,151] show increased spontaneous activity and responsiveness to noxious and innocuous joint movement in primary afferent fibers of Groups II, III, and IV. Similar changes occur following inflammation of the muscle with carrageenan [11,45] or following ischemia of the muscle [113]. Following peripheral inflammation, silent nociceptors begin to respond to both innocuous and noxious stimuli, such as pressure and joint movement (Fig. 2-2). Brennan and colleagues [74,130], using a model of postoperative pain, show a decrease in threshold and an increased responsiveness to cutaneous mechanical stimuli, as well as a small increase in receptive field size of the neuron (Fig. 2-2), thus indicating sensitization of the cutaneous nociceptors in response to injury. Taken together, these data indicate a general increase in the activity of nociceptors after tissue injury, which would increase the number of afferents firing after a peripheral insult and increase input to the CNS. This sensitization increases the responsiveness of primary pain afferent nociceptors to noxious stimuli and hence constitutes an explanation for hyperalgesia at the site of injury (i.e., primary

hyperalgesia) [145].

NEUROTRANSMITTERS OF PRIMARY AFFERENT FIBERS

Many neurotransmitters, receptors, and ion channels located within or on the peripheral terminals of primary afferent fibers are capable of producing pain and inflammation. Neurotransmitters in primary afferent fibers have been identified, predominately in neurons located in the DRG that send axons to the periphery. In some cases, neurotransmitters and receptors have been located within the peripheral terminals. Mediators of the inflammatory process can also activate primary afferent nociceptors to initiate the nociceptive or painful response to injury. This field has expanded tremendously in the last decade, with continued advances occurring exponentially. Therefore, we will only touch the surface of the pharmacology of peripheral nociceptors, highlighting a few well-established mechanisms. For a more extensive review, see [39,64,145].

Neuropeptides

Although blood-borne factors are considered to be the major initiator of inflammation, a substantial literature beginning in the late 1800s is devoted to the involvement of the peripheral and sympathetic nervous systems in this process (see [175,206]). **Neurogenic inflammation** is a term used to describe the role of the nervous system in the development and maintenance of peripheral inflammation. Neuropeptides such as substance P and calcitonin gene-related peptide (CGRP) are contained in small-diameter afferents (Groups III and IV). When released from primary afferent fibers in the periphery these neuropeptides produce an inflammatory response [12,15,97,101,205,211], indicating that primary afferent neurons are involved in plasma extravasation during arthritis. In fact, substance P and CGRP are increased in the inflamed knee joint [5,97]. Further, peripherally, there are changes in the content of fibers labeled for substance P and CGRP in both human inflammatory conditions and in animal models of inflammation [107,108,128]. Elimination of primary afferent fibers by peripheral neurectomy or capsaicin (which kills Group IV afferents) reduces the inflammatory response [33,93,94,166]. This neurogenic component of inflammation also involves the CNS through the generation of an action potential in the spinal cord that is transmitted to the periphery, termed dorsal root

reflex. This dorsal root reflex releases neuropeptides from the peripheral terminal to enhance the inflammatory response [140,141,172,174].

Opioids

Interestingly, after peripheral inflammation, in animals and human subjects, there is an upregulation of opioid receptors on the peripheral terminals of primary afferent fibers [184,186,187]. Additionally, macrophages, monocytes, and lymphocytes all contain endogenous opioid peptides [134], and the amount of endogenous opioid peptides in these cells in inflamed tissues increases [186]. In people with knee joint inflammation (osteoarthritis, joint trauma, and rheumatoid arthritis [RA]), there is expression of opioid peptides in immune cells and opioid receptors in primary afferent fibers in synovial tissue. Further, after knee surgery, blockade of opioid receptors with naloxone injected intraarticularly enhances pain and analgesic consumption [185]. Thus, there appears to be a peripheral endogenous mechanism to reduce pain in inflamed tissues. Further, the effects of opioid agonists, such as morphine, could produce their actions through activation of peripheral opioid receptors.

Glutamate

Glutamate is an important excitatory neurotransmitter in the nervous system, is found in primary afferent fibers [203], and its receptors are found on peripheral terminals of nociceptors [20,22]. Injection of glutamate peripherally produces hyperalgesia in humans and animals, and sensitizes primary afferent fibers [20,52,84,99,125,191]. Glutamate is upregulated in joint afferents after inflammation [204], and glutamate in inflamed tissues from humans and animals increases [98,110]. Further, the proportion of nociceptors expressing glutamate receptors increases after inflammation [21], and blockade of glutamate receptors reduces pain and hyperalgesia in human subjects and animals [19,23]. Clinically, increases in glutamate have been reported in temporomandibular disorder and myofascial pain of trapezius muscle [63,156].

Ion Channels

Several ion channels, found on peripheral terminals of primary afferent fibers, may also be important in the response to noxious stimuli. Low pH is found in inflamed tissues, is released in response to fatiguing exercise, and produces pain

in humans and animals [60,75,139,165]. *Acid-sensing ion channels* (ASICs) are located in DRG neurons, activated by low pH, and are importantly involved in pain from muscle and joint [67,83,116,133,167,169,171,176]. ASICs in DRG increase after inflammation of muscle or joint, and blockade of ASICs reduces the hyperalgesia associated with inflammatory and noninflammatory pain [176]. ASIC3 has been extensively studied and plays a significant role in musculoskeletal pain (for review, see [164]).

The vanilloid receptor-1, *TrpV1*, is activated by the exogenous ligand capsaicin, located in DRG, responds to low pH, and mediates hyperalgesia to heat stimuli [24,25]. In humans, intradermal or intramuscular injection of capsaicin produces pain and unpleasantness [208]. Further, inflammatory mediators can activate and sensitize TRPV1 through multiple second messengers, making it more responsive to peripheral stimuli such as heat or acid [145]. Clinically, low-dose capsaicin creams (<1%) are effective for treatment of neuropathic and musculoskeletal pain conditions such as postherpatic neuralgia and osteoarthritis [4]. Higher concentration patches are also used, 8% capsaicin, for treatment of neuropathic pain [4]. These treatments are thought to desensitize the nociceptors and produce a localized loss of nerve fiber terminals in the skin [4].

Sodium channels are involved in fast synaptic transmission and action potential propagation. The DRG neurons express six different sodium channels, including sensory-neuron-specific sodium channels not present within other parts of the nervous system. The involvement of sodium channels in the peripheral nervous system is complex, but clearly important for both inflammatory and neuropathic pain (see [6,35,43,201]). $Na_v1.7$ and $Na_v1.8$ play critical roles in nociception [14,35,43,51]. A change in sodium-channel composition occurs after peripheral neuropathy, resulting in physiological changes that contribute to hyperexcitability of DRG neurons [65]. Mutations in the genes encoding for $Na_v1.7$ result in the painful syndrome erythermalgia and the paroxysmal extreme pain disorder. In contrast, people with a complete loss of functional $Na_v1.7$ have been reported to be insensitive to pain [14,43,44,51,65]. Local anesthetics, such as lidocaine, mediate their effects by blocking sodium channels, and future pharmaceutical agents may be aimed at specific channels such as $Na_v1.7$ or the $Na_v1.8$.

NONNEURONAL ACTIVATORS AND

INFLAMMATORY MEDIATORS

Many substances are released from inflammatory cells that can directly activate and/or sensitize primary afferent fibers. It is now well established that the **immune system**, and factors released from immune cells (e.g., cytokines, chemokines), plays a critical role in the generation of both acute and chronic pain. Evidence for mast cells, neutrophils, macrophages, dendritic cells and T cells shows their involvement in a variety of pain conditions [39], and for macrophages in the analgesia by nonpharmacological treatments like acupuncture and exercise [38,100] (for details, see Chapter 10). Substances released by immune cells include serotonin, bradykinin, prostaglandins, cytokines, and chemokines. Serotonin, released from platelets, activates muscle nociceptors and causes pain in humans [59,144]. Bradykinin, which is released from plasma after tissue injury and is present in inflammatory exudates, sensitizes nociceptors and produces pain and heat hyperalgesia in humans [26,47,91,92,106,124,129]. Prostaglandins are metabolites of the arachidonic acid cascade and are produced in response to tissue injury. Prostaglandins directly excite and sensitize nociceptors through receptors located on primary afferent fibers [28,29,150]. The nonsteroidal anti-inflammatories (NSAIDs) produce their effects by reducing prostaglandin production through inhibition of the enzyme cyclooxygenase, which is involved in the breakdown of arachidonic acid.

During inflammation, **cytokines** are released by infiltrating macrophages at the site of injury and synoviocytes in joints. The proinflammatory cytokines, including interleukins (IL-1β, IL-6) and tumor necrosis factor (TNFα), are increased in the synovial fluid from patients with arthritis; they sensitize primary afferent nociceptors and produce mechanical and thermal hyperalgesia [36,57,58,87,88,109,126,199,200]. Although the actions of each of these inflammatory mediators are described individually, many mediators act together to enhance the inflammation and/or hyperalgesia, producing a potentiated response. Blocking TNFα receptors or reducing available TNFα reduces hyperalgesia in animal models of inflammation and neuropathic pain [178–180]. Several clinically available drugs available to reduce TNF availability are now considered important disease-modifying drugs (DMARDs) for people with inflammatory arthritis [57,79,138]. Additional DMARDs targeting interleukin-1 and interleukin-6 have recently become available to treat inflammatory arthritis.

Nerve growth factor (NGF) is a neurotrophic factor that is produced by muscle and during tissue injury [3,77,209]. It directly activates and sensitizes

nociceptors through its TrkA (high affinity) receptors [81,117,177]. Injection of NGF in humans and animals produces long-lasting hyperalgesia and results in an upregulation of proteins involved in pain transmission including substance P, TRPV1, and $Na_v1.8$ [9,86,190]. Together, these changes in gene expression enhance excitability of the nociceptor and amplify the neurogenic inflammatory response. Clinical trials are currently being performed in people with a variety of chronic pain conditions using an antibody to NGF; promising results from Phase II clinical trials have been published for people with osteoarthritis and chronic low back pain [89,146,154,193]. However, the safety of the drug in Phase III trials is being carefully monitored because there are reports of enhanced joint destruction in the active arm of the study compared with the placebo arm.

Adenosine tripshosphate (ATP) is found and released from muscle fibers during exercise, keratinocytes, and synoviocytes [7,85,104,188]. When injected into human subjects, it causes pain, and when injected into animals, it causes hyperalgesia. ATP binds purinergic receptors (P2X), particularly $P2X_2$ and $P2X_3$, which are found on nociceptors, resulting in activation and sensitization [18,42,158] (Fig. 2-3). Combining ATP with lactate and decreased pH can produce a potentiated effect enhancing nociceptor activity, hyperalgesia, and pain in animals and humans [13,102,131,155].

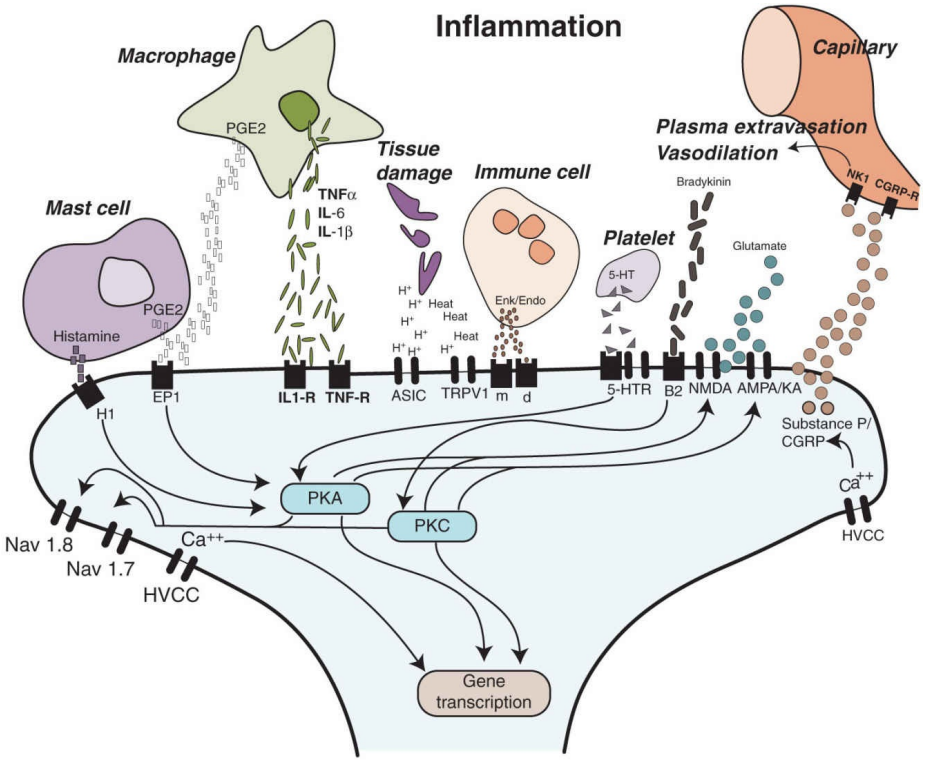

FIGURE 2-3 Schematic drawing of the peripheral mediators of sensitization

after inflammation. Release of a variety of neurochemicals from nonneuronal cells may act directly or indirectly to sensitize nociceptors. Release of substance P, CGRP, or glutamate can further enhance the inflammatory response by acting on nonneuronal cells and capillaries to cause plasma extravasation and vasodilatation. NK1, neurokinin-1 receptor; CGRP, calcitonin gene-related peptide; NMDA, *N*-methyl-D-aspartate receptor; AMPA/KA, non-NMDA glutamate receptors; IL, interleukin; TNF, tumor necrosis factor; PKA, protein kinase A; PKC, protein kinase C; ASIC, acid-sensing ion channel; H1, histamine 1 receptor; B2, bradykinin 2 receptor; 5-HT, serotonin; Enk/Endo, enkephalins and endomorphins; m, μ-opioid receptor; d, δ-opioid receptor; EP1, prostaglandin receptor; PGE2, prostaglandin E2.

ANIMAL MODELS OF PAIN

Several animal models of pain exist, are utilized to measure effectiveness of pharmaceutical agents, and mimic clinical conditions (for review see [53]). Animal models of pain can serve to probe the mechanisms behind the development and maintenance of different pain conditions. They also allow investigators to assess initial efficacy and safety of pharmaceutical and nonpharmaceutical treatments, as well as the mechanisms of action of these treatments. Models exist for studying cutaneous pain, neuropathic pain, musculoskeletal pain, visceral pain, and postoperative pain. These models can broadly be classified as acute pain models, inflammatory pain models, noninflammatory pain models, and neuropathic pain models. In general, nociception is measured in animals with reflexive tests examining withdrawal to noxious stimuli to indicate hyperalgesia and allodynia, and nonreflexive tests that indicate spontaneous pain, activity levels, and avoidance behaviors. Much of our knowledge on pain pathways, peripheral sensitization, and central sensitization has arisen from studies using these animal models of pain. For a more detailed description of animal models and outcome measures, see recent reviews [41,69,115].

Acute Pain Models

Acute pain models generally involve testing responses to noxious heat, mechanical or thermal stimuli in an uninjured animal. Such models have served for decades as screening tools to test the efficacy of pharmacological agents [56].

They do not typically result in tissue injury and thus do not cause hyperalgesia or neuron sensitization.

Cutaneous Pain Models

Generally, cutaneous pain models involve inflammation induced by injection of an irritant either into the skin or subcutaneously. Hyperalgesia is routinely assessed at the site of inflammation. These models of tissue injury were initially developed to more directly measure pain that might be similar to clinical syndromes. The most common inflammatory models involved injection of carrageenan or complete Freund's adjuvant (CFA) into the paw to produce an acute or chronic inflammatory event, respectively, resulting in primary hyperalgesia [143]. Animals show increased responses and decreased thresholds to mechanical and thermal stimuli after the induction of the inflammation [53,142]. In addition, the animals guard their limbs, decreasing the amount of weight-bearing on the inflamed extremity. Capsaicin, the substance found in hot chili peppers, activates TRPV1 channels and produces a local inflammation, as well as hyperalgesia. This substance has been used in both animals and human subjects as an experimental model of pain [50,95,159,162,208]. All cutaneous pain models result in peripheral and central sensitization of neurons in the nociceptive pathway, which includes nociceptors, dorsal horn neurons, and thalamic, cortical, and descending pathways [70,72,73,82,105,160]. Formalin is an inflammatory irritant that produces spontaneous pain behaviors that last for up to 1 hour [1]. This test produces two phases of behaviors, Phases I and II, that are thought to represent changes in the peripheral and central nervous system, respectively [1]. The formalin test has proven useful for screening pharmaceutical agents as well as for deciphering peripheral and central mechanisms.

Joint Pain Models

The most common model of joint pain involves injection of a mixture of kaolin and carrageenan into the knee joint [32,173]. This model mimics arthritic conditions and produces an acute, as well as a chronic, inflammatory phase [137]. This model is associated with primary hyperalgesia to mechanical pressure applied to the knee joint, secondary heat and mechanical hyperalgesia of the paw, limb guarding, avoidance behaviors, and decreased activity levels [132,137,161,194]. As inflammation becomes more chronic, hyperalgesia

spreads to include the contralateral hind limb [137]. Intra-articular injection of CFA and capsaicin also are used to model inflammatory joint pain [48,162]. Inflammation of the joint results in peripheral as well as central sensitization of dorsal horn, thalamic, amygadalar, and cortical neurons [49,70,71,122,123,147].

Models of osteoarthritis have been developed that involve injection of an irritant (monosodium acetate) that enhances joint destruction, or surgically by severing the anterior cruciate ligament of the knee or performing a diskectomy of the temporomandibular joint [103,198]. These models show limb guarding and hyperalgesia, along with joint destruction.

A model of repetitive strain injury has been developed where rats are trained to pull on a bar with or without force four times per minute, 2 hours/day, 3 days/week for up to 12 weeks [31]. This model results in increases in inflammatory cytokines around the median nerve, and changes in substance P and neurokinin-1 in the dorsal horn [8,54].

Models of RA involve injection of collagen type II antibodies (CAIA) or serum from K/BxN transgenic mice [30,171,198], and mimic the pathology of RA with widespread inflammation with the greatest effect distally, synovitis, cartilage degradation, and elevated inflammatory cytokines in the joint fluid. These RA models are associated with enhanced mechanical sensitivity of the paws and joints as well as reduced physical activity levels [171,189].

Muscle Pain Models

The most common model of muscle pain is induced by injection of carrageenan into a muscle belly to mimic myositis [112,137]. Similar to that observed for joint injection of carrageenan, there is an initial acute inflammation that converts to chronic inflammation [137]. The acute inflammation phase is associated with a unilateral primary and secondary hyperalgesia, whereas the chronic inflammation phase results in more widespread hyperalgesia that includes the contralateral hind limb [137]. Inflammatory muscle pain also results in peripheral sensitization of Group III and IV afferents, as well as central sensitization of neurons in the spinal cord dorsal horn [80,111].

A noninflammatory model of musculoskeletal pain was developed to mimic chronic widespread pain observed clinically in people with low back pain or fibromyalgia. Repeated intramuscular acid injections are noninflammatory but produce long, lasting mechanical hyperalgesia. Importantly, in this model there is no damage within the muscle or nerve tissue, and the hyperalgesia is maintained by changes in the CNS [165]. There is bilateral hyperalgesia of the muscle, paw as well as visceral hyperalgesia [114,165,192,212]. This model is

unique and does not result in peripheral sensitization, but is maintained by changes in the CNS that include sensitization of dorsal horn neurons and supraspinal pathways [165,168,192].

In view of the increased pain caused by an acute bout exercise in people with musculoskeletal pain [37,96,182], animal models have been developed to mimic this phenomenon. An acute bout of exercise in combination with a low-dose muscle insult results in long-lasting mechanical hyperalgesia that is widespread and enhanced in female mice [68,163,170,213]. Similarly, combining stress or inflammatory mediators with muscle insult enhances and prolongs hyperalgesia [27,66,135,136]. Thus, multiple models exist that mimic the conditions associated with chronic muscle pain.

Neuropathic Pain Models

Several models of neuropathic pain have been developed and are used extensively in animal studies. The most common models are (1) sciatic nerve ligation: induced by making loose ligations around the sciatic nerve [10], (2) spinal nerve ligation: induced by making tight ligations around the spinal nerves [90], and (3) spared nerve injury: tight ligation of the tibial and peroneal nerve in the hind limb [40]. Each of these neuropathic pain models produces a measurable long-lasting hyperalgesia and changes in the peripheral and central nervous systems [10,40,90]. Further models of neuropathic pain induced by chemotherapy drugs or by diabetes also result in long-term hyperalgesia [202,210]. Neuropathic models result in sensitization of nociceptors, as well as central pathways that include the dorsal horn and supraspinal sites [17,127,157].

Visceral Pain Models

Visceral pain models include hollow organ distention with and without inflammation and urinary bladder inflammation as models for generic visceral pain, irritable bowel syndrome, and cystitis, respectively [55,119]. Colorectal distention in awake, unanesthetized, unrestrained rats produces a quantifiable aversive behavior and cardiovascular and visceromotor responses indicative of acute visceral nociception [120]. After visceral inflammation or injury, there is sensitization of visceral nociceptors, sensitization of dorsal horn neurons and supraspinal modulation sites [34,61,62,118,121].

Postoperative Pain

To study postoperative pain, Brennan and colleagues developed an animal model in which a longitudinal incision is made through the skin, fascia, and muscle [16]. This model reflects both superficial and deep-tissue injury seen with surgery treatments, and results in spontaneous pain and mechanical hyperalgesia around the site of injury. Nociceptor sensitization and sensitization of dorsal horn neurons occur in response to incisional pain [74,130,214].

SUMMARY

This chapter has described the peripheral nociceptors innervating a variety of tissue types and the adequate stimuli that are necessary to activate them. Tissue injury may cause changes in these nociceptors that include increases in spontaneous activity, increased responsiveness to noxious stimuli, and a decreased threshold to noxious stimuli. This process of peripheral sensitization involves the neurotransmitters and receptors located in nociceptors, as well as inflammatory mediators. A variety of animal models are used to study clinical pain conditions and the underlying mechanisms for these conditions. The use of these animal models has greatly enhanced the understanding of a variety of painful conditions, spurred the development of new pharmaceutical and nonpharmaceutical treatments, and increased our understanding of the efficacy and mechanisms of current treatments. The next chapter will discuss the nociceptive pathways and neurotransmitters in the CNS and explore the changes that occur in animal models of pain.

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CHAPTER 3

Central Nociceptive Pathways

Kathleen A. Sluka

The processing of nociceptive information and pain in the central nervous system (CNS) is complex, involving multiple anatomical pathways and brain sites. These pathways include reflexive responses that are coordinated within the spinal cord, ascending nociceptive pathways, descending facilitatory pathways, and descending inhibitory pathways. All of these are interrelated and control the level of pain at a given time. Thus, pain processing is plastic and modifiable.

According to the classical "3-neuron system" described in neuroscience textbooks, transmission of nociceptive and temperature information involves the primary afferent fiber (first neuron), spinothalamic tract (STT) neuron (second neuron), and the thalamocortical neuron (third neuron) (Fig. 3-1). Regarding large-afferent sensation, this system involves the primary afferent fiber relaying information to the ipsilateral nucleus cuneatus and gracilis in the medulla (first neuron). Neurons in the nucleus cuneatus and gracilis transmit information to the contralateral ventroposterior lateral (VPL) nucleus of the thalamus (second neuron) and then on to the somatosensory cortex (third neuron). As will become apparent, this 3-neuron system is overly simplified for transmission of nociceptive information. This chapter will describe spinal, supraspinal, and cortical processing of nociceptive information.

SPINAL CORD

The spinal cord is the first site of termination of nociceptors in the CNS and integrates incoming information from primary afferent fibers, local spinal neurons, and supraspinal sites. The spinal cord is anatomically divided into 10 laminae [147] that correlate with function. Laminae I–VI comprise the dorsal horn, where most of the sensory afferents terminate. In general, the fine sensory

fibers conveying noxious information from the skin terminate in the most superficial layers, laminae I, II, as well as lamina V. The terminals of larger fibers conveying tactile information are dispersed between laminae III and IV. Many of these fibers terminate on spinal interneurons that then relay information to cells deeper in the spinal cord. Primary afferent fibers from several peripheral structures (the skin, joints, muscles, and viscera) may converge on one neuron (Fig. 3-1). This convergence is thought to be the basis for referred pain.

The central projections from neurons innervating muscles and joints are distinctly different from those innervating skin as described above. Muscle and joint send nociceptive information predominantly to lamina I and the deeper dorsal horn, in contrast to those from cutaneous tissue, which have dense projections to lamina II [37,119,120,157].

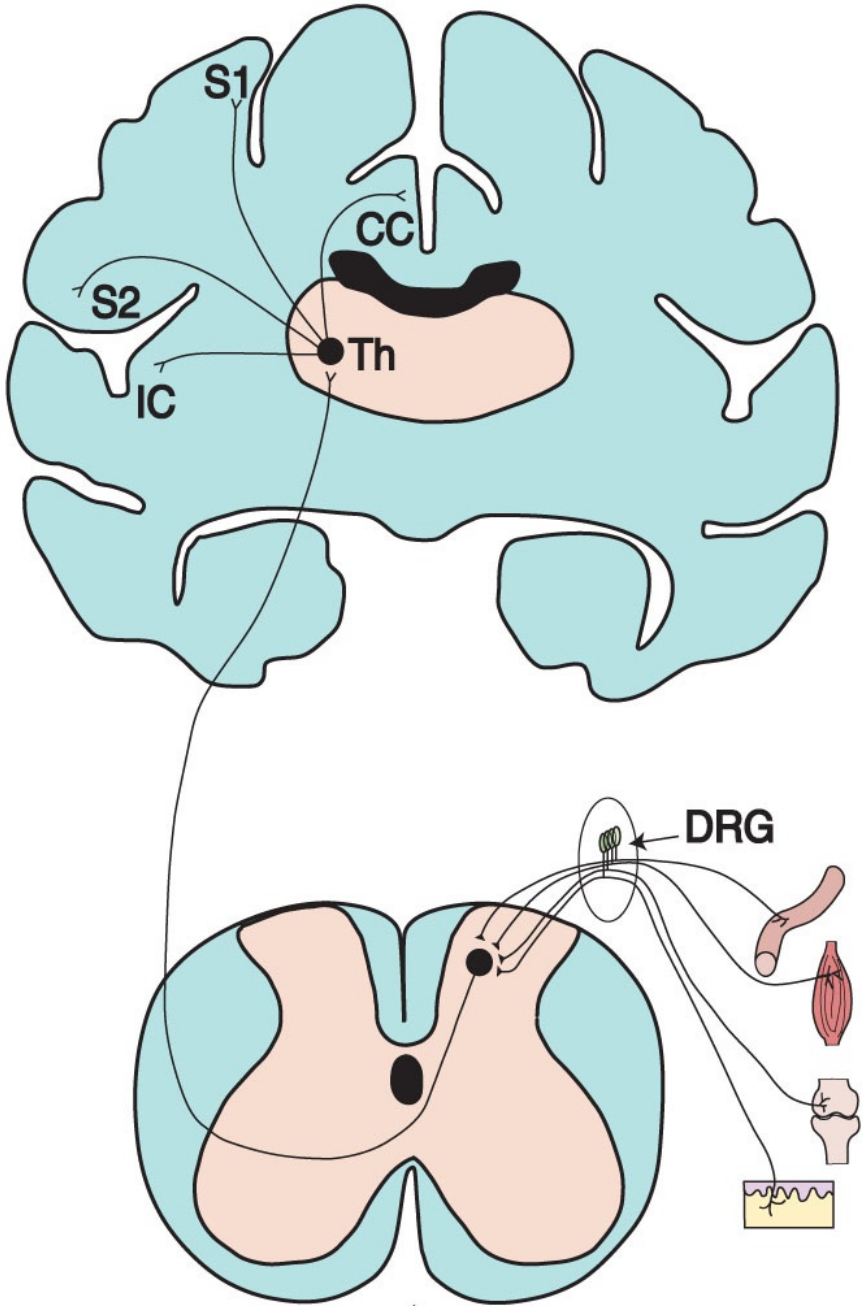

FIGURE 3-1 Illustration of the convergence of nociceptive input from different tissue types in the periphery on dorsal horn neurons. Multiple tissue types, skin, muscle, joint, or viscera, can send input to the same dorsal horn neuron in the spinal cord. The nociceptive input is conveyed to a spinothalamic tract neuron in the dorsal horn that then conveys nociceptive information to the thalamus. From the thalamus, nociceptive information is conveyed to the cortex. DRG, dorsal root ganglia; Th, thalamus; S1, primary somatosensory cortex; S2, secondary somatosensory cortex; IC, insular cortex; CC, cingulate cortex.

Neurons in the dorsal horn of the spinal cord are classified as high-threshold, wide dynamic range (WDR), and low-threshold neurons. High-threshold neurons respond only to noxious stimulation, low-threshold neurons respond only to innocuous stimuli, whereas WDR neurons respond to both noxious and innocuous stimuli. Thus, transmission of nociceptive information through the dorsal horn activates high-threshold and WDR neurons. After tissue injury, sensitization of both high-threshold and WDR neurons occurs, termed **central sensitization**. This condition is manifested as an increase in receptive field size, increased responsiveness to innocuous or noxious stimuli, and/or decreased threshold to innocuous or noxious stimuli [88,91,134,159]. Unique to central neurons is an increased responsiveness to innocuous stimuli after tissue injury, which is probably the underlying basis for **allodynia**, a painful response to normally innocuous stimuli.

Enlargement of receptive fields occurs after tissue injury and can include the entire limb or even the contralateral hind limb. For example, Schaible et al. [130,159] showed that within hours after induction of joint inflammation by injection of kaolin and carrageenan, the receptive fields of spinal dorsal horn neurons enlarge to include the entire hind limb (Fig. 3-2). In a noninflammatory model of muscle pain, the receptive fields enlarged to include the contralateral hind limb (Fig. 3-2), which parallels the bilateral hyperalgesia observed in this model [176]. Interestingly, Hoheisel et al. [88] showed that within minutes, injection of the inflammatory irritant bradykinin outside the neuron’s receptive field resulted in new receptive fields that included the site of injection, as well as additional sites (Fig. 3-2). Thus, expansion of receptive fields of central neurons is common and widespread, and it may explain the underlying referred and distant pain associated with deep tissue injury.

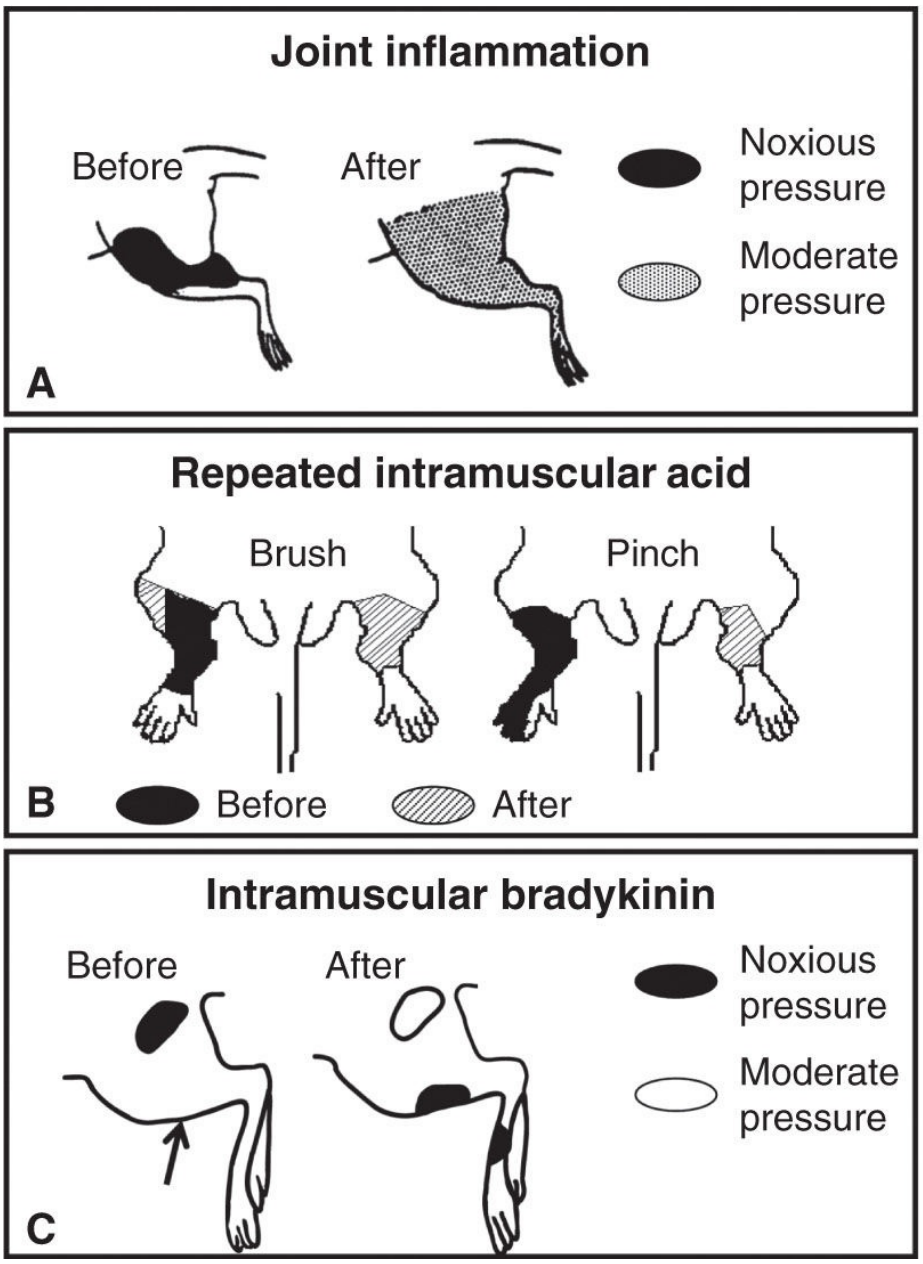

FIGURE 3-2 Extracellular recordings from dorsal horn neurons before and after injury to deep tissue. The receptive fields were assessed by application of stimuli to the periphery. **A:** Receptive field changes in response to inflammation of the joint with kaolin and carrageenan. Prior to inflammation, noxious pressure applied to an area around the knee joint evoked activity in the dorsal horn neuron. After joint inflammation, moderate pressure evoked activity in the dorsal horn neuron across the entire hind limb. (Reproduced from Neugebauer et al. [130] with permission of the American Physiological Society.) **B:** Responses of a wide dynamic range neuron to innocuous brushing and noxious pinching of the skin before (*black*) and after (*diagonal hatching*) the second injection of acidic

saline into the gastrocnemius muscle. The receptive field increased ipsilaterally and spread to the contralateral limb after the second injection for responses to both innocuous (*brush*) and noxious (*pinch*) stimuli applied to the skin. (Reprinted from Sluka et al. [176] with permission of IASP.) **C:** The receptive field of a dorsal horn neuron after intramuscular injection of bradykinin expanded to include the area of injection, as well as another area on the paw. In addition, the original receptive field showed a decreased threshold to activation, with moderate pressure now producing activity in the dorsal horn neuron. (Adapted from Hoheisel et al. [88] with permission of Elsevier, Inc.)

Sensitization of dorsal horn neurons, including STT neurons, to peripherally applied noxious and innocuous stimuli also occurs after tissue injury. Sensitization occurs not only in response to stimuli applied to the site of injury, but also after stimulation of uninjured tissue [48,130,159,218]. For example, recording from WDR neurons in the spinal cord, Neugebauer et al. [130] reported a progressive increase in firing rate in response to compression of the knee joint, or the ankle after knee joint inflammation (Fig. 3-3). Similarly, recording STT neurons show enhanced responsiveness to cutaneous noxious and innocuous stimuli after joint inflammation [48]. It should also be pointed out that changes occur not only in the dorsal horn neurons but also in motor neurons, as was shown in the original report of central sensitization [218,219]. Further, electrical stimulation of muscle nociceptors produces a longer-lasting and more robust response of central neurons than stimulation of cutaneous nociceptors [206].

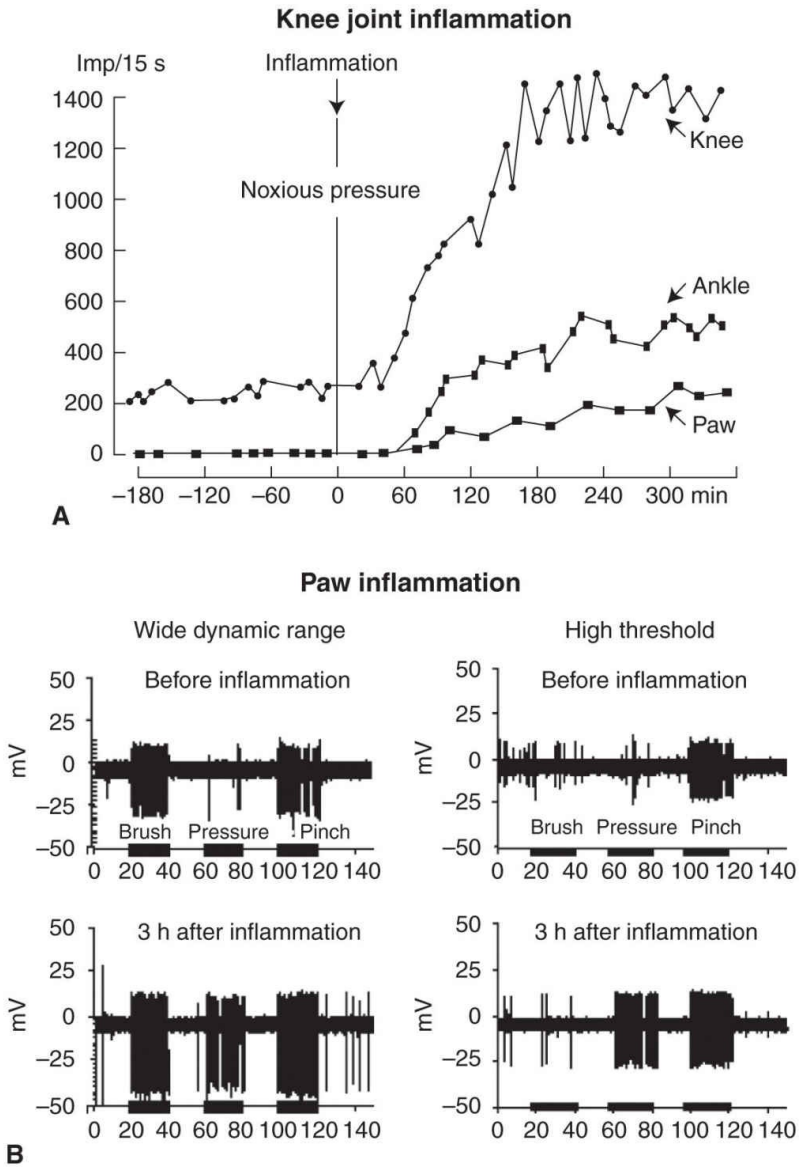

FIGURE 3-3 **A:** Extracellular recordings from dorsal horn neurons in response to noxious pressure of the knee, ankle, or paw before and after knee joint inflammation. After induction of knee joint inflammation *(arrow)*, the dorsal horn neuron developed an enhanced response to noxious pressure applied to the ankle and paw. (Reproduced from Neugebauer et al. [130] with permission of the American Physiological Society.) **B:** Recordings from wide dynamic range neurons and high-threshold neurons before and 3 hours after paw inflammation. Responses to innocuous *(brush)*, and noxious *(pinch)* differentiated the two types of neurons. Paw inflammation was followed by an increase in response to all stimuli, innocuous brushing, moderate pressure, and noxious pinch, for the wide dynamic range neuron. The high-threshold neuron showed increases in moderate pressure and noxious pinch after paw inflammation. (Reproduced from Ma and

Sluka [113] with permission of Springer.)

Sensitization of dorsal horn neurons can be maintained by input from sensitized nociceptors. In this case, the goal of therapy is to reduce the input from peripherally sensitized nociceptors, which will decrease sensitization of dorsal horn neurons and the consequent pain. However, central sensitization can be initiated by input from sensitized nociceptors and can persist in the absence of nociceptive input. For example, early studies showed that central sensitization and contralateral hyperalgesia induced by cutaneous insult continues after application of local anesthetics to the site of injury or deafferentation of the limb [31,32,221]. Similarly, the hyperalgesia associated with repeated intramuscular acid injections is independent of nociceptive input (which was removed by dorsal rhizotomy, or by local anesthetic injected into the muscle into which the acid was injected) [174]. If the central sensitization predominates and remains after peripheral injury, treatments should focus on central mechanisms to reduce central sensitization.

Glial Cells and Pain

Glial cells in the CNS, particularly the spinal cord, play a critical role in the processing of nociceptive information (for review see references [125,192]). Glia express receptors for many neurotransmitters including glutamate receptors and are involved in the clearance of neurotransmitters from the synaptic cleft. Activation of astrocytes and microglia (considered macrophages of CNS) occurs in many pain models including neuropathic and inflammatory models and facilitates nociceptive processing [59,63,192,194]. Interestingly, glia release a variety of neuroactive substances known to sensitize neurons such as glutamate, nitric oxide, and proinflammatory cytokines. Proinflammatory cytokines administered spinally produce nocifensive behaviors and sensitize dorsal horn neurons [41,145], and spinal blockade of proinflammatory cytokines reverses hyperalgesia [208] (Fig. 3-4). Further tissue injury reduces glutamate transporter expression on glia, leading to decreased glutamate uptake and enhanced excitatory transmission [191,195]. Glia can also have beneficial outcomes in the CNS and respond and contribute to the local immune environment. These benefits include release of anti-inflammatory factors, like IL-10, that restore normal nociceptive processing [125,182]. In addition to changes in the spinal cord, more recent studies show alterations in glial cells in brainstem and cortical areas involved in nociceptive processing [73,152,224]. Thus, glia play a significant role in both the facilitation and the inhibition of nociceptive

information in the CNS.

NEUROTRANSMITTERS OF THE SPINAL CORD

For an extensive review of the neurotransmitters and receptors involved in nociceptive transmission in the spinal cord, see [185,199,215]. A schematic diagram showing the neurotransmitters and their receptors is shown in Fig. 3-4.

Glutamate

Glutamate mediates excitatory synaptic transmission between primary afferent nociceptors and dorsal horn neurons [161,162]. The role of spinal ionotropic glutamate receptors in hyperalgesia resulting from tissue injury has been well established [29]. In particular, *N*-methyl-D-aspartate (NMDA) glutamate receptors, calcium channels with a voltage-dependent Mg^{2+} block, are implicated in synaptic plasticity in a variety of systems including nociceptive transmission [30]. Spinal application of antagonists to NMDA glutamate receptors decreases hyperalgesia associated with hind paw inflammation, joint inflammation, acid-induced muscle pain, formalin injection, and neuropathic pain models [18,33,117,146,170,180]. Blockade of spinal NMDA glutamate receptors prevents “wind-up” of both dorsal horn neurons and α-motor neurons, resulting in repetitive conditioning stimuli at C-fiber strength [40,45,220]. Furthermore, sensitization of dorsal horn neurons, including STT cells, that occurs after joint inflammation, formalin, capsaicin, or ultraviolet irradiation is prevented by NMDA-receptor antagonists [25,47,130]. The NMDA receptor has multiple subunits, NR1, NR2A, NR2B, that form the receptor complex. Each of these subunits can show enhanced expression, phosphorylation, and removal or blockade of these subunits can reduce pain behaviors in neuropathic, inflammatory, and noninflammatory animal models of pain [11,61,62,74,207].

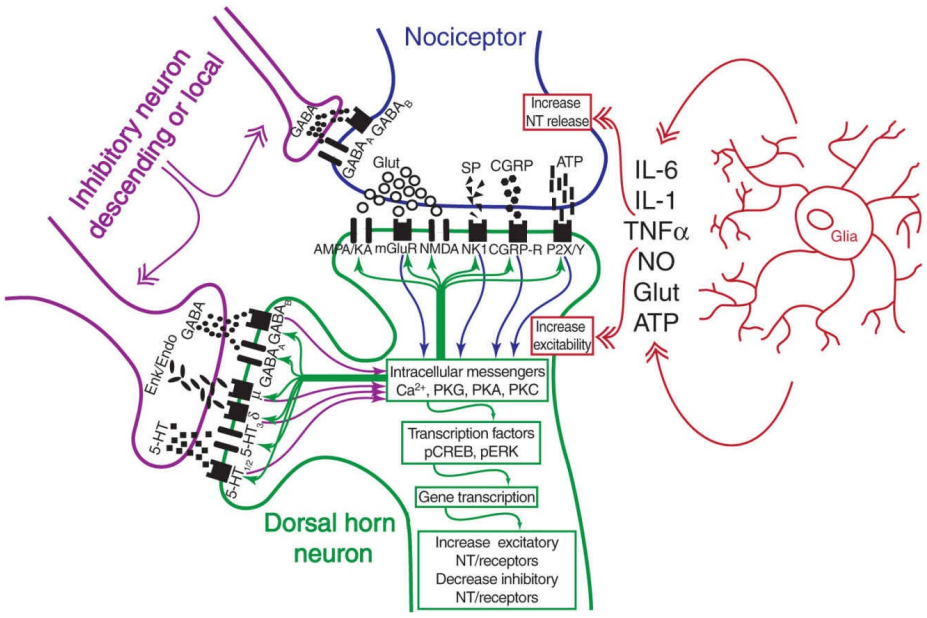

FIGURE 3-4 Schematic representation of the dorsal horn. Glial cells can be activated by noxious stimuli and release inflammatory cytokines and neurotransmitters to act on the central terminals of nociceptors or dorsal horn neurons, increasing neurotransmitter release and excitability. This increase in excitability can occur through activation of intracellular messengers that then phosphorylate cell surface receptors, or through phosphorylation of transcription factors. Phosphorylation of receptors can cause increased excitability or decreased inhibition to result in central sensitization. Changes in gene transcription can increase the production of excitatory neurotransmitters and receptors or decrease the production of inhibitory neurotransmitters and receptors, which would be manifested as central sensitization. Either local or descending inhibitory control can occur both presynaptically on nociceptors and postsynaptically on dorsal horn neurons, and can again produce its effects directly on membrane currents, through phosphorylation of receptors, or through activation of gene transcription. IL-6, interleukin-6; IL-1, interleukin-1; TNFα, tumor necrosis factor alpha; NO, nitric oxide; Glut, glutamate; ATP, adenosine triphosphate; Enk/Endo, Enkephalin/Endomorphin; GABA, γ-aminobutyric acid; SP, substance P; CGRP, calcitonin gene-related peptide; NK1, neurokinin-1 receptor; AMPA/KA, non-NMDA glutamate receptors; NMDA, *N*-methyl-D--aspartate; mGluR, metabotropic glutamate receptors; NT, neurotransmitter; PKG, protein kinase G; PKA, protein kinase A; PKC, protein kinase C; pCREB, phosphorylated cAMP responsive element binding protein; pERK, phosphorylated extracellular signal–related kinases.

The non-NMDA ionotropic glutamate receptors—AMPA and kainite

(AMPA/KA) receptors—form a complex with cation channels that allow passage of sodium ions, but some are also permeable to calcium, depending on subunit composition [90]. These AMPA/KA receptors are thought to mediate fast excitatory synaptic transmission between primary afferent fibers and dorsal horn neurons in response to noxious stimulation. Data are mixed on the role of AMPA/KA receptor antagonists in the development and maintenance of hyperalgesia. AMPA/KA receptor antagonists have no effect on hyperalgesia following carrageenan-induced paw inflammation once developed [146,186]. In contrast, for knee joint inflammation, noninflammatory muscle pain, peripheral neuropathy, and burn injury, hyperalgesia is reduced by spinal administration of AMPA/KA receptor antagonists [117,170,173,180,186]. Lastly, Zahn et al. [228,229] showed that hyperalgesia associated with incision is preferentially reduced by AMPA/KA receptor antagonists, but not NMDA glutamate receptor antagonists. As with NMDA receptors, several subunits of the AMPA/KA receptors, GluR1-4, can be upregulated and modulated in animal models of pain [185]. Thus, several models and conditions are sensitive to AMPA/KA receptor antagonists.

Although there are many selective NMDA receptor antagonists, these agents cannot be used clinically because of adverse side effects. However, several clinically available drugs, including ketamine, dextromethorphan, and memantine, have NMDA antagonist activity. These drugs are not selective antagonists, but block the NMDA receptor noncompetitively [212]. A clinical trial using dextromethorphan for postoperative pain shows lower opioid analgesic intake when compared with placebo [53].

Neuropeptides

The neuropeptides substance P and calcitonin gene-related peptide (CGRP) are found in the central terminals of primary afferent fibers and are densely located in laminae I and II (for review see reference [124]). Substance P exerts its effects through activation of the neurokinin-1 (NK1) receptor in the superficial dorsal horn. Activation of the NK1 receptor produces nocifensive behaviors [213], increases the activity and responsiveness of dorsal horn neurons [142], and potentiates the NMDA glutamate receptor [49]. In contrast, blockade of neurokinin receptors reduces hyperalgesia associated with tissue injury and reduces sensitization of dorsal horn neurons [58,132,141,175,226]. Further loss of NK1 containing neurons in the spinal cord similarly reduces hyperalgesia and sensitization of dorsal horn neurons following tissue injury [97,193]. Similarly, CGRP antagonists reduce sensitization of dorsal horn neurons [131]. In addition,

CGRP slows the degradation of substance P in the spinal cord [158], resulting in a potentiation of the effects of substance P. Interactions between receptors can potentiate responses. For example, spinal application of substance P in combination with CGRP greatly enhances the effects of either neuropeptide alone [222].

Adenosine

Adenosine is a neurotransmitter located in the dorsal horn of the spinal cord that exerts inhibitory actions through the A1 receptor [183]. Spinal administration of adenosine, A1 receptor agonists, or drugs aimed at reducing the degradation of adenosine are analgesic and reduce hyperalgesia in inflammatory and neuropathic pain conditions [92,107,135,155,156]. In human subjects, modulation of adenosine in the spinal cord systemically reduces neuropathic pain [52,183].

γ-Aminobutyric Acid

γ-aminobutyric acid (GABA) is an inhibitory neurotransmitter located in neuronal cell bodies of the dorsal horn. It exerts its actions through activation of the ionotropic receptor, $GABA_A$, and the metabotropic receptor, $GABA_B$. GABA is upregulated by peripheral inflammation and decreased by peripheral neuropathy [7,23], and activation of GABAergic receptors in the spinal cord reduces hyperalgesia and causes analgesia [77,190]. One potential mechanism that may contribute to hyperalgesia is a reduction in GABAergic inhibition. For example, STT cells show a reduced responsiveness to GABA agonists after induction of inflammation with capsaicin [111]. Clinically, several muscle relaxants (such as baclofen and benzodiazepines) exert their effects through activation of GABA receptors.

Intracellular Messengers

Protein kinases mediate intracellular processes through the phosphorylation of receptors, cellular proteins, or transcription factors (Fig. 3-1). Phosphorylation of intracellular receptor proteins enhances the transport of these excitatory receptors to the cell membrane, thus making the cell more sensitive to ligands, whereas phosphorylation of transcription factors can initiate gene transcription and subsequently increase the expression of nociception-related proteins.

In the spinal cord, activation of protein kinase A (PKA) or protein kinase C (PKC) produces mechanical hyperalgesia, sensitizes STT neurons, and phosphorylates transcription factors to enhance gene production [86,111,112,122,171,172,178,181]. Furthermore, blockade of PKA or PKC pathways in the spinal cord reverses mechanical hyperalgesia and dorsal horn neuron sensitization associated with deep tissue inflammation, repeated acid injections, or neuropathic pain [86,116,171,234,235]. Interestingly, PKC phosphorylates ionotropic channels such as the NMDA and AMPA/KA receptors that enhance glutamate-evoked currents on dorsal horn neurons [24]. This phosphorylation by PKC removes the Mg^{2+} block in the NMDA receptor pore to increase the probability of the channel opening [26]. Mitogen-activated protein kinases (MAP-kinases) and the extracellular signal–related kinase (ERK) have emerged as key intracellular messengers in nociceptive processing in the CNS, including the spinal cord [93]. Changes occur in both neurons and glia in a number of animal models of pain. Thus, increased phosphorylation of glutamate receptors could enhance synaptic activity, resulting in increased excitation of nociceptive dorsal horn neurons.

Alternatively, activation of intracellular messengers can phosphorylate inhibitory neurotransmitter receptors to result in a decrease in efficacy of inhibitory neurotransmitters. PKC reverses μ-opioid receptor inhibition in the spinal dorsal horn of rats, leading to decreased μ-opioid receptor–mediated antinociception. PKC also decreases the ability of the inhibitory neurotransmitter GABA to inhibit STT cells [111]. Injection of capsaicin reduces the inhibition of STT neurons normally produced by electrical stimulation of the periaqueductal gray (PAG); this loss of inhibition is prevented by spinal blockade of PKC [110]. Thus, increased PKC activity reduces normal inhibition within the spinal cord, resulting in an increase in excitation.

Several transcription factors have been implicated in nociceptive processing in the dorsal horn, including CREB, nuclear factor-κB, and the immediate early gene FOS [93]. Increased expression or phosphorylation of these transcription factors in both neurons and glia have been shown in many animal models including neuropathic, inflammatory, and noninflammatory pain models [93]. Activation of these transcription factors leads to enhanced synthesis of proinflammatory and pronociceptive mediators, resulting in prolonged enhancement of pain [93].

Serotonin, Norepinephrine, and Opioids

Serotonin and norepinephrine are neurotransmitters found in descending projections from the brainstem, and endogenous opioids are also located in areas of descending inhibition and spinal cord (see the section below on descending inhibition).

ASCENDING PATHWAYS

From the spinal cord, sensory information is conveyed to the brain via projection neurons that receive inputs from afferents directly or indirectly through interneurons. Noxious information is considered to be relayed by cells that have been defined either as high-threshold neurons or WDR neurons. Several ascending pathways transmit nociceptive information from somatic and visceral tissue [215,216]. The STT is the main pathway for transmission of nociceptive information (relayed through the thalamus) to higher centers involved in cortical processing and ultimately in the perception of pain (Fig. 3-1). The postsynaptic dorsal column pathway transmits nociceptive visceral stimuli to higher centers. The spinomesencephalic and spinoreticular pathways serve to integrate nociceptive information with areas involved in descending inhibition, descending facilitation, and autonomic responses associated with pain.

Spinothalamic Tract

The pathway considered by many to be most important for the transmission of nociceptive information is the STT. The STT transmits information to neurons in the VPL nucleus and medial thalamic nuclei that include the central lateral, central medial, parafascicular, and medial dorsal and posterior complex of the thalamus. The VPL projects to the primary (S1) and secondary (S2) somatosensory cortex, and this pathway is thought to be involved in the **sensory–discriminative component of pain** (i.e., its location, duration, quality, and intensity). Neurons in the VPL receive convergent input from the dorsal column pathway that transmits information regarding touch sensation and the STT conveying information regarding pain and temperature sensation [96,215,216]. The ascending projections from the medial thalamic nuclei and the posterior complex are more diffuse and include areas such as the anterior cingulate and insular cortices. This pathway is thought to be the basis for the **motivational–affective component of pain** (i.e., its unpleasantness).

STT cells originate primarily in laminae I and V, with most of them crossing

the midline to ascend in the contralateral anterolateral funiculus [215]. The STT cells from lamina I project via the lateral and dorsolateral funiculi to the medial thalamic nuclei. These cells respond almost exclusively to noxious thermal and mechanical stimuli and may play an important role in thermal nociception [36]. It has also been suggested that this pathway may be responsible for activating the body's own control systems to limit pain [144,205,216]. Several investigators support a role for WDR STT cells, particularly those in lamina V, which respond to both nociceptive and mechanoreceptive stimuli [217]. Sensitization of WDR neurons to innocuous mechanical stimuli may underlie allodynia, a painful response to an innocuous stimulus.

Spinomesencephalic and Spinoreticular Tracts

Cells of the spinomesencephalic tract originate in laminae I, IV, and V and send projections to the midbrain, particularly the PAG, the nucleus cuneiformis, and the pretectal nucleus [215,216].These neurons are classified as high-threshold and WDR and have complex receptive fields. The projection to the PAG probably activates descending modulatory systems. The cells of origin of the spinoreticular pathways are located in the deep dorsal horn, laminae VII and VIII, and project to brainstem areas known to be involved in descending facilitation and inhibition of nociception. These nuclei include the nucleus gigantocellularis, nucleus paragigantocellularis lateralis, ventrolateral medulla, and parabrachial region. These neurons are nociceptive specific and are proposed to activate the endogenous analgesia system and signal homeostatic changes to brainstem autonomic centers.

Thalamus and Cortex

Many studies show the importance of the thalamus and the cortex in processing nociceptive transmission. These include studies recording and stimulating neurons in the human thalamus, recordings from thalamic and cortical neurons in animal models of pain, and imaging studies [71,72,87,104,143]. Stimulation of the principal sensory nucleus of the thalamus in humans can produce pain sensations, and thalamic neurons in humans respond to noxious thermal or mechanical stimuli. Thus, the thalamus appears to integrate information regarding peripheral noxious stimuli. Recordings from neurons in animals show that nociceptive information is processed in the VPL of the thalamus as well as the somatosensory cortex, insular cortex, and anterior cingulate cortex (ACC).

Neurons in these thalamic and cortical areas become sensitized after inflammatory or neuropathic injury.

Brain Imaging

Central processing of pain in humans has been assessed with imaging techniques, such as functional magnetic resonance imaging (fMRI) and positron emission tomorgraphy (PET), that look at cerebral blood flow changes resulting from specific stimuli, and have been extensively reviewed [5]. Blood flow to an area is enhanced with increased neuronal activity. Hundreds of human brain imaging studies have examined cortical and subcortical processing of pain in healthy subjects. These data indicate a consistent pattern of activation that is sometimes referred to as the pain matrix. The regions most reliably activated by painful stimuli are S1 and S2, ACC, and insular cortex, prefrontal cortex, thalamus, and cerebellum [34,87,143]. Studies by Hofbauer et al. [87] and Rainville et al. [143] elegantly examined the role of the somatosensory cortex and cingulate/insular cortices using hypnosis to make suggestions that modulate the sensory–discriminative component of pain or the motivational–affective component of pain. Thus, the primary and secondary somatosensory cortices are involved in discrimination and localization of a painful stimulus (i.e., the sensory–discriminative component of pain) and the anterior insular and cingulate cortices mediate the unpleasantness of pain (i.e., the motivational–affective component of pain).

Studies in people with pain have shown similar patterns of activation to those with acute pain stimuli in healthy controls. Differences do exist and include generally less consistent activation of S1 and S2 in those with ongoing pain, greater activation of the prefrontal cortex, and increased amygdala activation [5]. In osteoarthritis patients with greater neuropathic pain symptoms, a greater activation of brainstem areas occurs [76]. In people withchronic pain conditions such as fibromyalgia chronic pain conditions such as fibromyalgia, generally greater activation of cortical sites occurs with the same noxious stimuli, and normally innocuous stimuli (in healthy controls) that now produce pain (in those with fibromyalgia) show activation of brain areas normally activated by pain [68].

Resting state fMRI is a relatively new tool used to explore the connectivity between functionally linked brain regions, and is used to examine brain networks (for review see reference [127]). The default mode network is defined as a network of brain regions active when an individual is resting but awake and not focused on the outside world (including the inferior parietal lobe, posterior

cingulate cortex, medial prefrontal cortex, hippocampus, and lateral temporal lobe). People with fibromyalgia experience altered processing in this default mode network with greater connectivity to the insular and S2 cortices from the default mode network, and increased connectivity between areas within the default mode network (prefrontal cortex and cingulate cortices).

Recent studies show that individuals with long-lasting pain conditions such as low back pain, fibromyalgia, and osteoarthritis have altered structural changes in the brain manifested as a decrease in gray matter density in pain modulating regions like the cingulate, insular, and prefrontal cortices [5]. Interestingly, several studies show that gray matter decreases return to normal after successful treatment [5,75]. Similarly, decreases in the neuronal marker *N*-acetylaspartate (NAA) are observed in the hippocampus, thalamus, and prefrontal cortex in people with chronic pain, and relate to pain severity. What the decreases in gray matter or NAA represent is unclear, but they are not likely related to cell death as they reverse with successful treatment.

Neurotransmitters including opioids and glutamate can also be imaged in the brain. Increased levels of glutamate in the insular cortex have been observed in people with fibromyalgia and migraine [5,81], and these increases were decreased after treatment in people with fibromyalgia [82]. For opioids, several studies show decreased binding of opioids in people with a variety of pain conditions, including neuropathic pain and fibromyalgia [46,80,94,114], which may help explain the reduced effectiveness of opioids in people with these chronic pain conditions.

DESCENDING MODULATION OF PAIN

Descending modulation of nociceptive information occurs through several nuclei, including the PAG, the rostral ventromedial medulla (RVM), and the lateral pontine tegmentum (Fig. 3-5). These sites were initially found to inhibit nociception through projections either directly or indirectly to the spinal cord [57,123]. Later studies showed a role for these structures in descending facilitation of nociception [138]. Anatomically, the PAG sends projections to the RVM and the lateral pontine tegmentum, but not directly to the spinal cord. The RVM and lateral pontine tegmentum then project to the spinal cord and modulate dorsal horn neuron activity and ultimately nociceptive information. Activation of descending pathways likely occurs through cortical sites like the cingulate cortex, insular cortex, prefrontal, and amygdala, which all send input directly to

the PAG. Extensive reviews of central pain modulation are available for more information [85,128].

Clinical studies often test conditioned pain modulation (CPM), referred to as diffuse noxious inhibitory controls (DNIC). The pathways for CPM and DNIC are unique and involve activation of the reticularis dorsalis nucleus in the medulla that subsequently projects to the spinal cord; the PAG and RVM are not involved in this inhibition [12–14,42] (see below). There is a balance between facilitation and inhibition from these descending modulatory pathways. This balance shifts after tissue injury in a time-dependent manner to result in a net output manifested as either increased facilitation or increased inhibition.

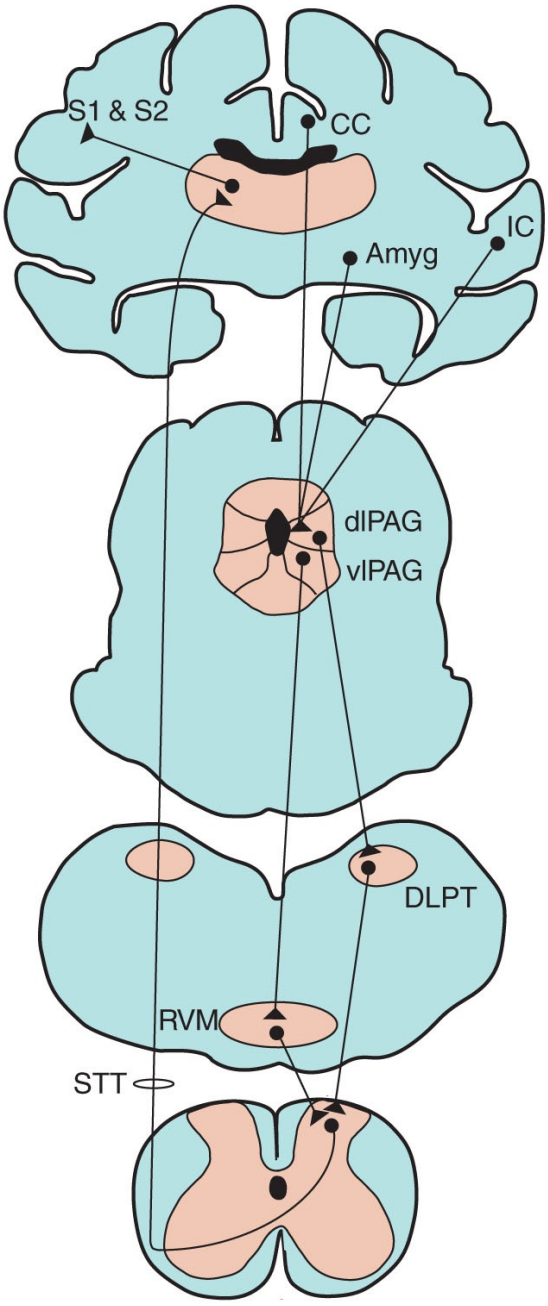

FIGURE 3-5 Schematic representation of the descending inhibitory and facilitatory pathways; and the spinothalamic tract. S1 and S2, somatosensory cortex 1 and 2; CC, cingulate cortex; IC, insular cortex; Amyg, amygdala; dlPAG, dorsolateral periaqueductal gray; vlPAG, ventrolateral periaqueductal gray; DLPT, dorsolateral pontine tegmentum; RVM, rostroventromedial medulla; STT, spinothalamic tract.

Descending Facilitation of Pain

Supraspinal centers can enhance nociception, resulting in referred pain, secondary hyperalgesia, and “mirror-image” or contralateral hyperalgesia [138]. Inactivation of the RVM completely blocks secondary hyperalgesia produced by knee joint inflammation, repeated acid injections, pancreatitis, or neuropathic injury [17,35,197,198,201,203]. Interestingly, these manipulations in the RVM do not affect the primary hyperalgesia produced by carrageenan injected into the plantar paw [201]. Similar to the findings observed for the spinal cord, increased glutamate release, phosphorylation of NMDA glutamate receptors, or increase in the number of NMDA glutamate receptors occurs in the RVM after tissue injury [70,74,140,197,231]. More rostrally, the PAG, pontine nuclei, amygdala, and ACC also play a role in descending facilitation [20,44,89,129]. The facilitation by many of these nuclei is likely mediated through the RVM. Thus, supraspinal centers play a major role in the production and maintenance of hyperalgesia.

As pain is an emotional as well as a sensory experience, multiple brain sites are involved in processing and facilitation of pain. The amygdala has emerged as a critical site in processing nociceptive information. It is classically involved in emotion and fear and directly projects to the prefrontal cortex. Recent studies show that connections between the amygdala and the prefrontal cortex are altered or sensitized in animals with inflammatory, neuropathic and visceral pain conditions [38,98,128,129]. The ACC is also involved in nociceptive processing, in particular, the escape and avoidance of noxious stimuli [60]. Animal studies show increased activity of neurons in the ACC during escape from noxious stimuli and that lesioning the ACC eliminates avoidance behaviors to noxious stimuli, but leaves sensory withdrawal reflexes to noxious stimuli intact [60]. Similarly, human subjects with cingulectomy decrease the affective dimension of pain without altering the sensory components of pain [60]. Thus, distinct and multiple brain areas modulate different dimensions and consequences of pain.

Descending Inhibition of Pain

The central inhibitory control of pain was initially discovered by Reynolds [148], who found that electrical stimulation of the **PAG** in the midbrain produces analgesia in rats. Early work focused primarily on two sites, the midbrain PAG and a site in the ventral medulla, the nucleus raphe magnus (NRM). Subsequent studies show that other nuclei in the **RVM** are similarly involved in descending modulation of nociceptive information. These nuclei include the NRM, nucleus reticularis gigantocellularis pars alpha, and nucleus reticularis paragigantocellularis lateralis [9,57,84] (Fig. 3-5). Electrical or chemical stimulation of either the PAG or the RVM causes analgesia in rats, cats, and

humans [50,55,64,108,148], and inhibits spinal neurons that respond to noxious stimuli [1,55,84,105,109,151,232]. The PAG does not project directly to the spinal cord, but rather projects to the RVM [21]. The RVM, in turn, projects to the spinal cord via fibers running in the dorsolateral funiculus. Efferent projections from the RVM to the spinal cord are involved in inhibition of nociception, and some of the projections contain serotonin [96,169].

In addition to the PAG and RVM, other nuclei in the brain also inhibit pain and nociception when activated. These include anterior pretectal nucleus, locus coeruleus/A7 cell groups, hypothalamus, somatosensory cortex, thalamus, red nucleus, medial habenula, parabrachial region, hypothalamus, prefrontal cortex, amygdala, reticulospinal tract, and rubrospinal tract [39,43,69,79,84,129,149,165,177,216]. Most of these sites relay either directly or indirectly through the RVM, with the RVM serving as the final common pathway to the spinal cord.

RVM Neurons Involved in Inhibition and Facilitation of Pain

Three types of neurons located in the RVM play a role in descending nociceptive modulation, as described in rat studies using noxious heat applied to the tail: (1) *ON cells*, which increase their firing rate just before or at the time of tail flick; (2) *OFF cells*, which decrease their firing rate just before or at the time of tail flick, and (3) *Neutral cells*, which do not respond consistently to noxious heat applied to the tail (Fig. 3-6) [56,84]. OFF cells are thought to be involved in descending inhibition, whereas ON cells are thought to be involved in descending facilitation of nociceptive information. Morphine, a μ-opioid agonist, excites OFF cells and reduces nocifensive behaviors when applied directly to neurons in the RVM, or the PAG, or when administered systemically. Conversely, morphine or deltorphin, a δ-opioid agonist, will suppress ON cell firing [78,84], thus attenuating nociceptive responsiveness (Fig. 3-6). Interestingly, removal of ON cells in the RVM, with dermorphin–saporin, prevents facilitation of nociception in animals with neuropathic pain [137]. Activation of the RVM in facilitation and inhibition of pain occurs in a time-dependent manner, depending on the animal model tested [17,196,202]. Further, RVM neurons can alter their phenotype in animals with tissue injury, with neutral cells developing either ON-like or OFF-like activity after induction of inflammation [121]. Thus, RVM neurons play a critical role in both the inhibition and the facilitation of pain, and tissue injury can alter their response properties.

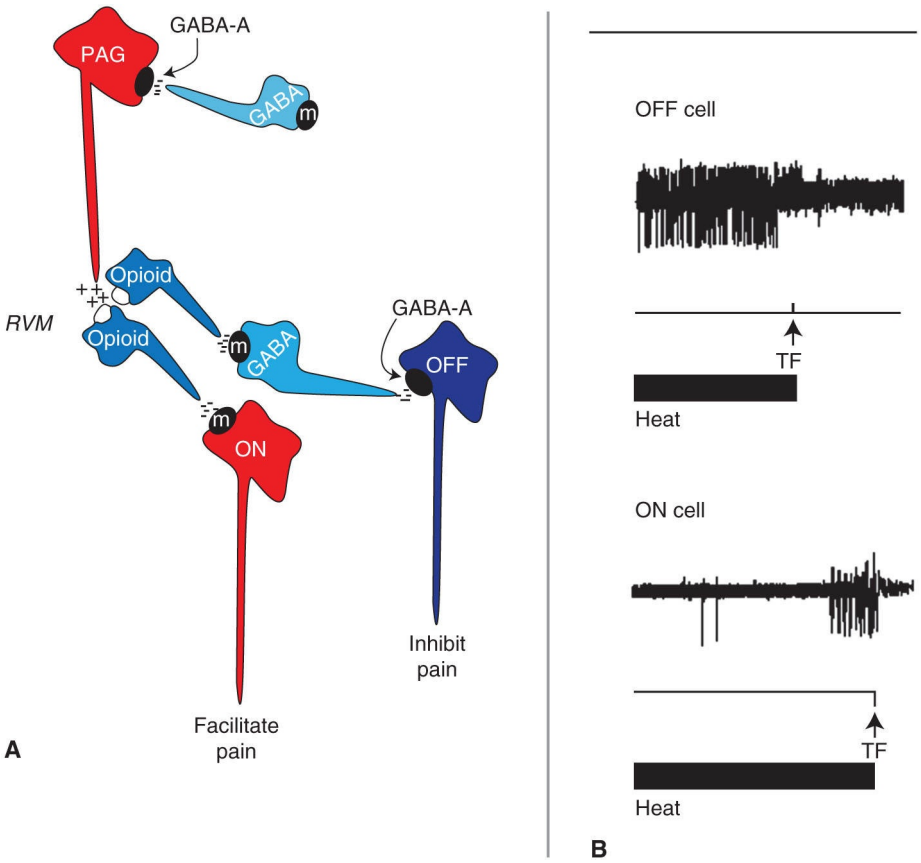

FIGURE 3-6 **A:** Schematic diagram of cells in the periaqueductal gray (PAG) and rostroventromedial medulla (RVM). Activation of OFF cells is thought to inhibit pain, whereas activation of ON cells is thought to facilitate pain. Projections from the PAG excite opioid cells in the RVM that activate μ-opioid receptors on ON cells, which inhibits these cells, thus decreasing facilitation. Some ON cells are GABAergic and tonically inhibit OFF cells. Activation of m-opioid receptors on these GABAergic ON cells can then reduce the GABAergic inhibition of OFF cells, resulting in increased activity in OFF cells that would inhibit pain. **B:** Representative recording of OFF cells and ON cells in response to noxious heat applied to the tail. The OFF cells stop firing in response to noxious heat as measured by the tail flick (TF). The ON cell begins to fire immediately prior to the tail flick in response to noxious heat. (Reprinted from Fields et al. [57] with permission from Elsevier.)

The **dorsolateral pontine tegmentum** (DLPT) sends projections to the spinal cord primarily from the locus ceoruleus and nucleus subceoruleus. The DLPT uses norepinephrine as its neurotransmitter and serves as the primary source of norepinephrine in the spinal cord. Chemical or electrical stimulation of these nuclei causes antinociception, reduces hyperalgesia, and decreases the activity of spinal neurons [95,106,200,230]. Norepinephrine may inhibit or

facilitate nociceptive stimuli, depending on the activation of specific adrenergic receptors in the spinal cord (see the neurotransmitter section).

In addition to receiving nociceptive input for the discrimination of pain, this somatosensory cortex also sends fibers that inhibit nociceptive transmission, either directly to the spinal cord via the **corticospinal tract** or indirectly through the thalamus or PAG. Stimulation of the somatosensory cortex inhibits STT neurons [166,227] and causes primary afferent depolarization, resulting in presynaptic inhibition [22]. Lesioning of the corticospinal tract blocks the primary afferent depolarization produced by stimulation of the somatosensory cortex, demonstrating that presynaptic inhibition of the central terminals of primary afferent fibers can be mediated by activation of the corticospinal tract [22]. Thus, stimulation of the corticospinal tract (as with exercise) may reduce nociceptive input through the inhibition of spinal neurons or primary afferent fibers. Clinically, emerging evidence shows that stimulation of the motor cortex with transcranial magnetic stimulation (TMS) can reduce pain in patients with neuropathic pain, phantom limb pain, chronic low back pain, and fibromyalgia [4,103,118,167].

DNIC is a term used to describe an innate pain modulatory system in which the application of noxious stimuli induced generalized analgesia. DNIC can be demonstrated experimentally by the application of painful stimuli to an extrasegmental site, which produces analgesia at the test site. For example, application of a noxious stimulus (heat or cold) to the arm increases the pressure pain threshold of the leg in normal subjects [204]. Activation of DNIC pathways reduces hyperalgesia and pain in both animals and human subjects, and also reduces dorsal horn neuron activity [204]. The analgesia produced by DNIC is opioid mediated and involves pathways outside the PAG–RVM pathway [42,204]. By mechanisms not fully understood, the reticularis dorsalis nucleus in the medulla appears to mediate the analgesia produced by activating DNIC pathways [204]. DNIC-like analgesia is commonly tested in people with chronic pain and is referred to as CPM [225]. Studies in people with chronic pain show less efficient CPM (i.e., decreased inhibition to a noxious stimuli) in conditions such as temporomandibular disorder, chronic low back pain, fibromyalgia, osteoarthritis, chronic tension-type headache, and irritable bowel syndrome [16,99,100,102,136,153,214].

NEUROTRANSMITTERS OF DESCENDING SYSTEMS

Opioids

After peripheral inflammation, in animals and human subjects, an upregulation of opioid receptors on the peripheral terminals of primary afferent fibers occurs [115,188,189]. Additionally, macrophages, monocytes, and lymphocytes all contain opioid peptides, and the amount of endogenous opioid peptides in these cells increases in inflamed tissues [115,188]. Thus, there appears to be a peripheral endogenous mechanism to reduce pain in inflamed tissues. The effects of opioid agonists, such as morphine, could produce their actions through activation of peripheral opioid receptors.

Opioid analgesia has been extensively studied in endogenous pain control mechanisms. The endogenous opioids include β-endorphins, methionine (met)- and leucine (leu)-enkephalin, endomorphin 1 and 2, and dynorphin A and B [57]. Each has a distinct anatomical distribution and activates specific receptors. There are three types of opioid receptor: μ, δ, and κ. β-endorphin and endomorphins activate the μ-opioid receptors, the enkephalins activate the δ-opioid receptors, and the dynorphins activate the κ-opioid receptor. β-endorphin is found in hypothalamic neurons and the anterior and intermediate lobes of the pituitary [57]. Neurons located in the hypothalamus send β-endorphin projections to the PAG and can “turn on” the endogenous analgesia system [210]. Release of β-endorphin from the pituitary occurs with exercise and stress, and an increase in measurable levels is found in the bloodstream [83,160,164]. β-Endorphins do not readily cross the blood–brain barrier, and thus their role in stress-induced or exercise-induced analgesia is not known. However, one could postulate that β-endorphin in the bloodstream produces its analgesic effects peripherally by activating μ-opioid receptors on nociceptors, in an upregulated manner after tissue injury, to reduce peripheral sensitization.

Enkephalins, endomorphins, and dynorphins and their receptors are located in neurons in the brain and dorsal horn in areas known to be involved in analgesia such as the PAG, RVM, and dorsal horn of the spinal cord [57,123]. Activation of opioid receptors with selective agonists, systemically or locally in the PAG, RVM, or spinal cord, produces analgesia and reduces hyperalgesia in many pain models including inflammatory pain, acid-induced muscle pain, and neuropathic pain [57,123,179,223].

Most of the clinically available opioids produce their effects through activation of μ-opioid receptors. Differences in effectiveness are based on potency of the drug. Clinically available opioids include morphine, codeine, tramadol, oxycodon, levorphanol, methadone, hydromorphone, buprenorphine, and fentanyl. Long-term clinical use of opioids is limited by the development of

tolerance to their analgesic effects [163]; clinical use and concerns are discussed in Chapter 15.

Serotonin

Serotonin is a neurotransmitter that is found in the RVM in neurons that send projections to the spinal cord, and in PAG neurons that project to the RVM [8,10,15]. Application of serotonin to the spinal cord decreases the activity of dorsal horn neurons and produces analgesia [123]. Downregulation of serotonin in the RVM, using RNAi technology, reduces inflammatory pain behaviors [211], suggesting that serotonin neurons in the RVM facilitates pain behaviors. Thus, it appears that the PAG pathway producing analgesia uses serotonin as its neurotransmitter in the spinal cord.

In the spinal cord, multiple families of serotonin receptors are present (5-HT1, 5-HT2, 5-HT3, 5-HT4, 5-HT5, 5-HT6, 5-HT7) and have been extensively reviewed [123]. The role of individual serotonin receptors and receptor subtypes in nociceptive transmission is controversial, because 5-HT receptors have been implicated in both facilitation and inhibition of nociception. 5-HT3 receptors, located on primary afferent fibers and dorsal horn neurons, are involved in descending inhibition from stimulation of the RVM but not in descending facilitation [2,65]. 5-HT3 receptors in the spinal cord have also been implicated facilitation of nociception through activation of glial cells. 5-HT1A receptors, on the other hand, are not found on primary afferent fibers; they mediate descending facilitation as well as inhibition [3,19,51]. 5-HT2 receptors include a number of subtypes that appear to be involved in inhibition, but not in facilitation, of nociceptive responses [184].

Norepinephrine

Norepinephrine (i.e., noradrenaline) terminals in the spinal cord arise primarily from the DLPT [28,123]. Spinally, norepinephrine inhibits nociceptive stimuli through activation of α_2-adrenergic receptors [67,101,139]. On the other hand, activation of spinal dorsal horn α_1-adrenergic receptors mediates descending facilitation of nociception [133]. Thus, norepinephrine is involved in descending facilitatory and inhibitory nociceptive signaling, depending on receptor activation.

Tricyclic antidepressants, dual reuptake inhibitors, or selective serotonin reuptake inhibitors (SSRIs) are commonly used for chronic pain conditions.

These inhibitors can be nonselective (amitryptaline, imipramine, duloxetine), exerting their effects by decreasing reuptake of norepinephrine and serotonin, or selective (fluoxetine, paroxetine, ritanserin, clomipramine), acting by decreasing reuptake of serotonin. A decrease in reuptake would result in greater neurotransmitter availability and increased inhibition of nociceptive information. Tricyclic antidepressants and SSRIs enhance antinociception and pain reduction in animals and humans [150,168,209]. Further, 5-HT1 agonists such as sumatriptan, zolmitriptan, naratriptan, and rizatriptan are effective for treating migraine [66,126].

POTENTIAL MECHANISMS OF CENTRAL SENSITIZATION

Sensitization of dorsal horn neurons can occur through multiple mechanisms that could include increased excitation or decreased inhibition. Short-term sensitization can result from increased release of excitatory neurotransmitters such as glutamate or substance P that consequently activate their receptor, depolarizing the neuron. Alternatively, decreased release of inhibitory neurotransmitters may also occur, which would result in an overall increased excitability of nociceptive neurons. More long-term effects can occur through phosphorylation of receptors. For example, PKC phosphorylates the NMDA receptor to remove the magnesium block, resulting in a greater response to its agonist glutamate [27]. On the other hand, phosphorylation of GABA receptors results in a loss of inhibitory effect by GABA on STT cells [111]. Lastly, increased gene transcription could result in more long-term effects that include production of more excitatory neurotransmitters or receptors. Indeed, increased phosphorylation of transcription factors, increased activation of transcription factors, and an increased number of glutamate receptors in the spinal cord occur after tissue injury [54,86,122,233].

CORRELATION OF NEURONAL CHANGES WITH PAIN MEASURES

Mechanisms underlying various pain types are distinctly different (see Table 3-1). **Primary hyperalgesia** is thought to reflect increased sensitivity of

nociceptors to noxious input (i.e., peripheral sensitization). Although changes occur in the CNS within minutes after tissue injury, and central neurons show an enhanced response to application of noxious stimuli to the injured tissue, this central sensitization most likely reflects the increased activity of the nociceptors. However, repetitive electrical stimulation of C fibers with the same intensity of stimulation, in animals without tissue injury, results in a progressively increasing activity of dorsal horn neurons, termed “wind-up” [40]. Assessment of **temporal summation** in human subjects is thought to reflect wind-up of dorsal horn neurons, and is used experimentally to assess the sensitivity of the CNS. Temporal summation is manifested as progressively increasing pain to repeated application of the same painful stimuli. Several pain conditions (e.g., temporomandibular disorder, fibromyalgia, and tension-type headache) result in enhanced temporal summation when compared with controls [6,154,187]. **Referred pain** is pain felt outside the site of tissue injury. It is not evoked by noxious or innocuous stimuli, as observed in hyperalgesia or allodynia. The *convergence–projection theory* is used to describe the mechanisms underlying referred pain. At the spinal level, neurons receive input from cutaneous as well as deep tissue such as muscles, joints, or viscera. The increased activity that results from injury to deep tissue is transmitted to the cortex, where it is misinterpreted as pain from the skin or another structure. Referred pain therefore reflects processing in the CNS. **Secondary hyperalgesia** could result from sensitization of dorsal horn neurons that occurs after tissue injury. Because central neurons have relatively large receptive fields that greatly expand after tissue injury, the increased response to noxious stimuli applied outside the site of injury is thought to be of central origin. Alternatively, or in conjunction, activation of facilitatory pathways from supraspinal sites can result in enlarged receptive fields and increased sensitivity of dorsal horn neurons to noxious stimuli applied outside the area of injury. Thus, the cortex interprets this increased input as pain in response to noxious stimuli outside the area of injury (i.e., secondary hyperalgesia) and reflects sensitization in the CNS. **Allodynia** most likely results from the increased responsiveness of STT neurons to innocuous stimuli. Under normal conditions, the response to innocuous stimuli of WDR neurons does not reach the threshold for pain perception. However, after tissue injury, the responses to innocuous stimuli are increased and reach a threshold that is interpreted in the brain as pain. Therefore, allodynia is a reflection of CNS neuron sensitization.

TABLE 3-1 **Behavioral Responses and Proposed Mechanisms**

Behavioral Manifestation	Definition	Proposed Site of Change	Proposed Mechanism of Change	Comments
Primary hyperalgesia	Increased pain sensitivity at the site of injury	Peripheral nervous system nociceptor	Peripheral sensitization	Can be manifested as deceased threshold to noxious stimuli, or as increased pain to a suprathreshold stimulus
Referred pain	Perceived pain outside the area of injury	CNS	Convergence–projection theory	Pain is perceived outside the area of injury; the term should not be used to describe an increased sensitivity to painful stimuli (this is termed hyperalgesia)
Secondary hyperalgesia	Increased sensitivity outside the site of injury	CNS	Central sensitization to noxious stimuli	Likely involves changes in the nociceptive pathway anywhere from the spinal cord to the cortex
Allodynia	Painful response to nonnociceptive stimuli	CNS	Central sensitization to innocuous stimuli	This term should be used only when it is known that the test stimulus does not activate a nociceptor
Temporal summation	Progressively increasing pain to the same stimulus administered repetitively or over a long duration	CNS	Wind-up of dorsal horn neurons	This is an assessment used in clinical pain studies to analyze the sensitivity of the CNS
Pain	An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms as such	CNS	N/A	Pain is a cortical evaluation of the response to a noxious stimulus (i.e., pain occurs only when processed by the cortex)

Abbreviation: CNS, central nervous system.

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CHAPTER 4

Motor Control and Pain

Paul W. Hodges

People can move differently in the *presence* of pain, when *threatened* by pain, after *resolution* of pain, or as a *precursor* to pain. In each scenario there could be relevance for such changes to be assessed and addressed with treatment. At first glance many changes appear straightforward, reasonable, and beneficial to the individual—for example, avoidance of full weight-bearing and dorsiflexion of the ankle during walking after an acute ankle sprain, co-contraction of trunk muscles to limit spine movement after provocation of pain [26], and so on. Yet these changes could equally be part of the problem—for example, increased muscle activation predicts recurrence of low back symptoms [8]. Changes could also be both beneficial and problematic; that is, changes that are logical in the early phase to protect a painful segment could become problematic for other body regions or problematic for the region it aims to help —for example, walking with external rotation of the leg after spraining an ankle would protect the injured ligament in the early phase by reducing the demand for ankle dorsiflexion, but would increase the demand for movement of proximal segments, and in the long term could lead to limited ankle mobility. Changes in motor control are not straightforward and not well explained by current theories.

Motor control refers to all of the motor, sensory, and information-processing elements associated with generation of motor functions [61]. Differences in any (or all) of these elements may be present in an individual with *present*, *previous*, or *threatened* pain. For the patient in pain, consideration of motor control may be critical for recovery, and to address these issues may be a major element of intervention. This chapter provides an overview of the contemporary view of motor control changes in pain, possible mechanisms, and potential benefits of treatments that aim to change the way a patient moves.

HOW DOES MOTOR CONTROL RELATE TO

PAIN?

Early theories proposed a simplistic relationship between pain and motor control: that pain would lead to either inhibition of muscle activity [75] or "spasm" [56]. This evolved into theories that predicted both inhibition and facilitation of muscle. The "pain adaptation" theory proposes inhibition of muscles producing a painful movement and facilitation of muscles that oppose it [43]. As many clinical and experimental observations do not align with these predictions of stereotypical response to pain, newer theories propose a more variable response that depends on the individual, the task, and the context [30,31,50]. However, fundamental to the changes in motor control in "pain" is the realization that there are several discrete, but interconnected, contexts in which changes/differences can be interpreted. In the contemporary clinical and experimental literature, there are four major ways in which changes in motor control are considered in conjunction with nociception/pain/injury and/or anticipation of pain/injury (Fig. 4-1):

1. Suboptimal movement/motor control as a **precursor** to injury and pain [8,57];
2. Impaired movement/motor control as a **consequence of interference** by actual or threatened injury and/or pain [27,62];
3. Modification of movement/motor control for **protection** of the painful/injured/threatened region [31]; and
4. Modified movement/motor control explained by a **conditioned association** with pain [49,51].

Each alternative may be associated with unique modifications of motor function, unique mechanisms, and unique outcomes for the health of the individual. Of course they may overlap—an adaptation to *protect* could be a *precursor* for other problems; and adaptation to *protect* could become *conditioned*. Each alternative may have different implications for management; different strategies may be required to change control, and whether or not it is beneficial to change control may depend on the underlying basis for the change. Each option requires consideration.

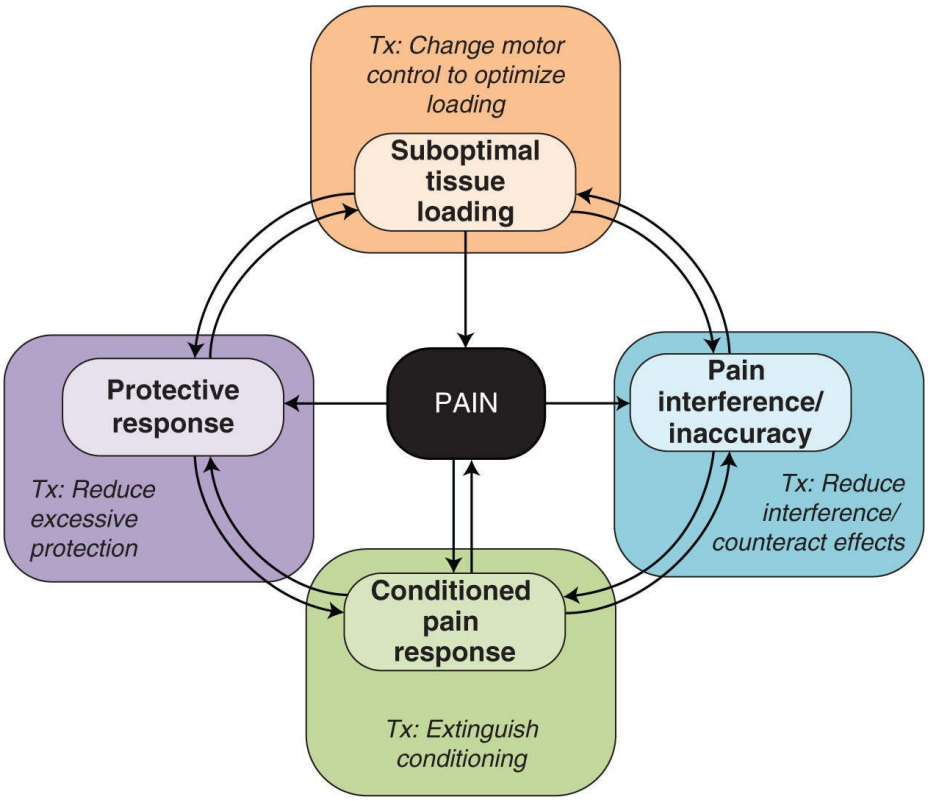

FIGURE 4-1 Interaction between pain and movement, and possible treatment targets. Pain and movement interact according to four hypotheses that are not mutually exclusive. Pain and/or injury (or threatened pain/injury) may change motor control by interference with motor output (negative) or by initiation of a protective solution (positive, in the short term). Movement may continue to be painful by suboptimal loading of tissues or if movement is conditioned to provoke pain in the absence of nociceptive input. Suboptimal loading of the injured or other tissues may lead to the onset of pain, or may be the result of pain interference or a negative consequence of the protective response. Different treatments *(Tx)*, highlighted in colored boxes, may be required to target the different features that link pain and movement.

Suboptimal Tissue-Loading Hypothesis

An individual may move/align his or her body or activate muscles in a manner that loads his or her tissues suboptimally (Fig. 4-2). This could be an initial precursor to development of pain/injury in the first instance [8,57], or a factor in its recurrence [24]. The fundamental basis of this hypothesis is that suboptimal tissue loading leads to excitation of nociceptive afferents (with or without tissue injury) and, ultimately, pain. Such process could be enhanced if the peripheral tissues or the neural pathways are sensitized by peripheral or central

sensitization, such that less input is required to initiate nociceptive discharge or activate the pain network. In this case repeated exposure to the suboptimal loading mechanism may provoke pain.

Single loading events with high force (e.g., slip or trip), unexpected force, or high loading in suboptimal positions induce tissue injury, nociceptive activation, and pain [5]. In these situations movement/motor control may be optimal but loading exceeds the capacity of the tissues. On the other hand, the view that accumulation of load *over time* from adoption of a strategy that loads the tissues suboptimally is less well defined or accepted. This concept has been proposed for many years (e.g., reference [17]), but empirical evidence has been limited. Many examples are cited in the clinical literature, such as "poor" posture/alignment (e.g., sitting in an end-range posture [11]), movement with poor alignment of the axis of rotation (e.g., axis of rotation of glenohumeral joint during shoulder motion [2]), or poor coordination of motion between adjacent segments (e.g., early motion of the spine, before the hip in leg movement tasks [60]; modified "start position" such as motion of the glenohumeral joint from a suboptimal position of rotation [47]). The primary argument against this proposal is that there are many people who use strategies that are deemed "negative," but are pain/injury free, and therefore questioning the relationship to nociceptive input/pain/injury. The counterargument is that for a specific movement/loading strategy to cross the "threshold" and induce nociceptive input/pain/injury there must be sufficient "exposure" [13]; whereas high forces can exceed tissue tolerance with as few repetitions as one, low forces may require repeated exposure over an extended period to exceed the threshold. Add to this potential individual variation in the resilience of tissues and psychosocial context, and the equation between loading strategy and pain/injury becomes complex. Furthermore, there will not one but multiple different loading strategies that could be problematic (e.g., sitting more flexed or more extended both present in people with pain [11]). Taken together, it is not surprising that not all individuals with a specific posture/alignment, movement, or muscle activation pattern present with injury and pain. Multiple factors must converge to exceed the threshold of tissue tolerance.

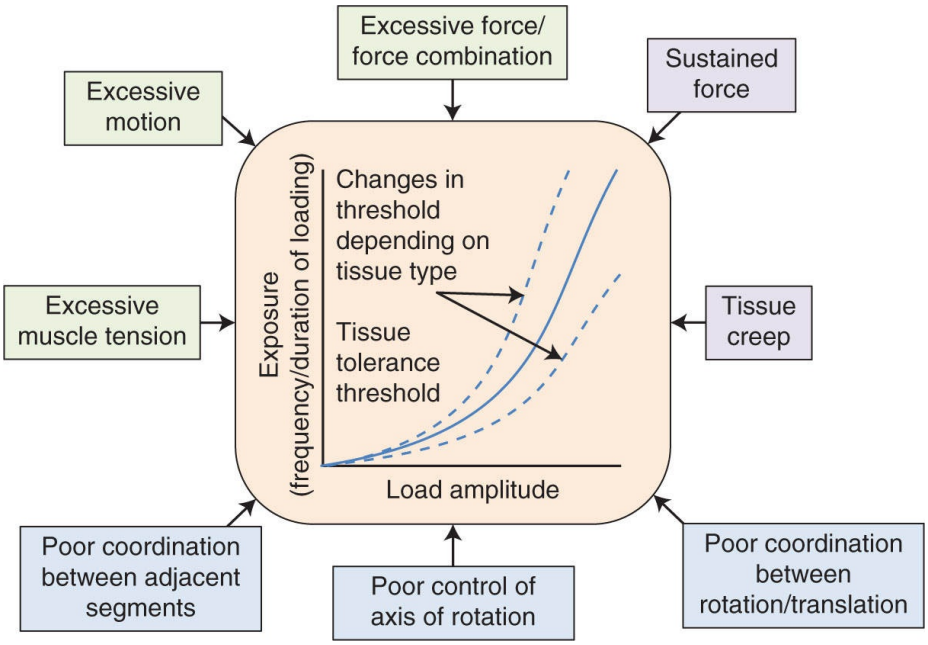

FIGURE 4-2 Suboptimal tissue-loading hypothesis. Whether loading of tissues exceeds the threshold for tissue health depends on the interaction between load amplitude and the exposure (frequency and duration). Tolerance may also depend on individual variation in tissue type/resilience. Suboptimal loading may take many forms. Although suboptimal loading may lead to initial onset of injury and pain, it may not be necessary for the maintenance of pain.

Why are suboptimal loading strategies adopted? Multiple theories have been presented. Some examples are as follows:

- **Habit**—habitual use of a specific pattern of movement, posture, or muscle activation;
- **Environmental factors**—poor posture motivated by a chair design, use of a computer [63]; modified hip mobility secondary to sustained periods sitting in posterior tilt;
- **Functional factors**—asymmetrical muscle development from frequent exposure to asymmetrical task (tennis playing [72]; cricket fast bowling [21]) leading to adoption of such patterns in other tasks;
- **Presumed benefit**—adoption of a posture or movement in response to information that this is beneficial (sitting with excessive thoracolumbar extension as the perceived ideal posture [9]);
- **Energy minimization**—adoption of posture or movement that are supported by passive resistance rather than muscle activity (e.g., standing in hip adduction supported by iliotibial band tension [22]);
- **Previous exposure to pain/injury**—motor adaptation induced by

pain/injury may remain [29,44] (see sections “Pain/Injury Interference Hypothesis” and “Protective Response Hypothesis” below).

This latter item is a rising theory in clinical management of pain—that an individual who has recovered from injury/painful event may have initially developed a modified motor control strategy in response to the event (pain may have motivated the change), but the adaptation may persist beyond the recovery of pain (although pain is a motivator to change, relief of pain does not necessarily motivate resolution to a “normal”/“optimal” motor pattern). In this case suboptimal loading secondary to the modified motor behavior could become a risk factor for the recurrence of pain. Some evidence exists. For instance, individuals who fail to recover the size of the multifidus muscle after an acute episode of back pain have a greater risk for recurrence of symptoms [24].

Regardless of the explanation for the adoption of a suboptimal motor control strategy, the assumption is that maintained “use” of the strategy continues to suboptimally load the tissues leading to nociceptor discharge. In the presence of peripheral or central sensitization, this would be amplified such that less stimulus/loading is required to activate the nociceptors (peripheral sensitization), or the signal may be amplified centrally (central sensitization)—the threshold for “pain” may be lowered or non-nociceptive afferent input activates the “pain” network [79]. It is critical to recognize that the relationship between nociceptive input and pain is not linear. Nociceptive input is neither *sufficient* nor *required* to maintain pain (see section “Conditioned Response Hypothesis” below). Normal sensation may be perceived as painful—either because of sensitization [79] or conditioned association with the pain experience [49]. Thus, experience of pain does not necessarily mean that loading is abnormal or that nociceptors have been activated. Furthermore, the intensity of pain does not accurately reflect the extent to which tissue is suboptimally loaded. The major consequence of this nonlinearity and the physiology of the pain network is that although modified movement may have *initiated* the pain experience, it may not be the reason it is *maintained*.

If suboptimal tissue loading continues to activate nociceptors, then changing movement to optimize the loading may be relevant for symptom recovery. However, because of the nonlinearity of the relationship between pain and loading, rehabilitation of movement patterns may not lead to symptom recovery, or may lead to recovery but not for the reasons presumed to be responsible.

Pain/Injury Interference/Inaccuracy Hypothesis

In addition to the potential for suboptimal motor control to lead to pain and injury, pain and injury clearly change motor control. Although from one perspective this may be viewed as a "protective" solution to reduce potential for pain and/or injury (see section "Protective Response Hypothesis" below), from another, injury/nociceptive discharge/pain or even the threat/anticipation of these, may change motor behavior in a manner that interferes with behavior leading to inaccuracy and does not necessarily serve an obvious role in protection. These mechanisms may act at any level of the nervous system (Fig. 4-3).

Nociceptive or non-nociceptive afferent input from injured tissue may directly influence excitability of motoneurons. Although nociceptive input is often presumed to have an inhibitory input to motoneurons, animal studies show that activation of nociceptive afferents in animals lead to both inhibitory and excitatory potentials on motoneurons [41]. The net effect is not straightforward, and both increased and reduced excitability has been shown in animal (increased discharge of masseter motorneurons after mustard oil application in rats [64]) and human studies (increased excitability of biceps motoneurons with hypertonic saline injection [46]).

Non-nociceptive afferent input, via interneurons, can inhibit and facilitate motoneurons. Reflex inhibition (sometimes referred to as "arthrogenic" inhibition) is independent of the effects "pain" and commonly inhibits extensor muscles (inhibited quadriceps muscle after knee injury [14,62]) with concurrent facilitation of flexor muscles (hamstrings [14]). This is argued to explain many changes in motor control after acute injury, including early atrophy of the multifidus muscle in acute back pain [25,27].

Disrupted peripheral sensory function can also interfere with motor control. Many possibilities exist. For instance, direct injury to a mechanoreceptor or the tissue within which the sensory receptor is located (e.g., muscle, ligament, joint capsule) will modify afferent input [12,54]. Depending on the extent of injury and the availability of other sensory information to compensate, this would compromise the awareness of position and movement. Nociceptive input and local chemical changes (e.g., local inflammation) can alter muscle spindle sensitivity [65].

Supraspinal motor and sensory mechanisms are also possible contributors. Acute nociceptive input and injury changes excitability of sensory and motor areas [42,59,69]. More sustained symptoms are related to changes in organization of the motor [66,67] and sensory [19] cortices. How these changes

may relate to modified motor function and whether this equates to “interference” or “protective” function, or both, remains unclear. Some data show compromised corticospinal inputs to specific muscles (e.g., hypertonic saline injection leads to reduced excitability of inputs to transversus abdominis, which is considered important for fine-tuning of spine motion [69]), but enhanced excitability of inputs to other muscles involved in *protective responses* (e.g., obliquus externus abdominis [69]).

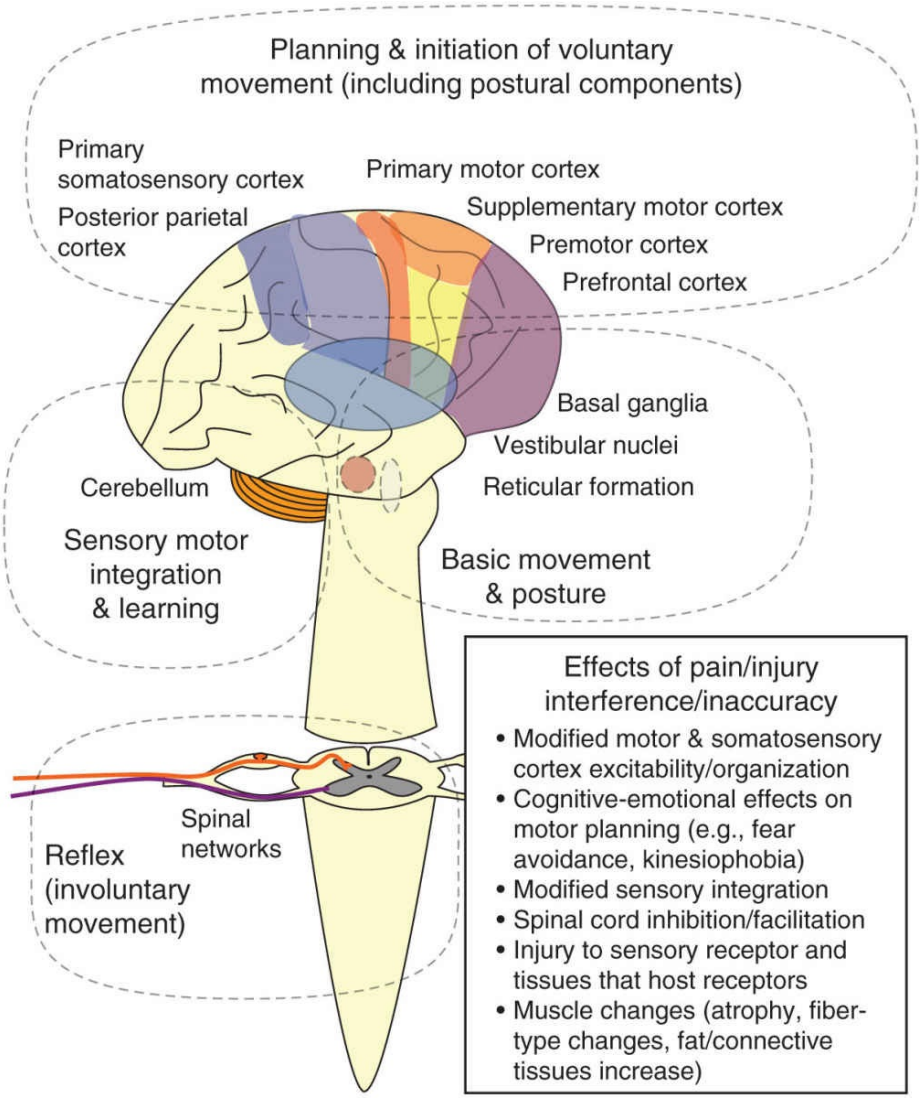

FIGURE 4-3 Pain/injury interference/inaccuracy hypothesis. Pain and injury may interfere with motor output at any level of the sensorimotor system. The sensorimotor system occupies a substantial area of the nervous system, and different regions contribute to different features of motor function, broadly according to the detail in the figure. Pain and injury have been shown to have effects on motor output at each of the sites highlighted. At these sites,

nociceptive or non-nociceptive afferent input, or descending input from higher centers (molded by beliefs, attitudes, and expectations) may compromise the quality of motor control, leading to interference with function, or suboptimal loading of tissues.

There is also extensive evidence of muscle changes (atrophy, muscle fiber-type changes, fatty infiltration, connective tissue changes [3,15,25,28]) associated with pain/injury. Although chronic changes in muscle may have a straightforward mechanism related to disuse [1], the nature of changes and the underlying mechanisms in acute and subacute periods are debated [3,25]. Recent work proposes different mechanisms with different time courses: reflex inhibition in the early phase; a possible role for inflammatory system in the intermediate period; and disuse in the chronic phase [28]. Regardless of the mechanism, and despite the "intention" of the nervous system to perform a specific motor function, the muscle apparatus may not be able to meet this demand.

Regardless of the mechanism, the maladaptive effect of pain/injury on motor output may compromise function, may predispose to further pain/injury, or may be an epiphenomenon (i.e., change in motor function that is present but with no direct relevance for persistence or recurrence of pain). To counteract interference/inaccuracy it may be necessary to target the stimulus for the effect (e.g., joint swelling), the outcome of the interference (e.g., reflex inhibition), or both.

Protective Response Hypothesis

In the context of acute pain, the basic premise of the adaptation in motor control is that it serves to protect the tissues from further pain and/or injury (Fig. 4-4). In response to information regarding threat to the tissues (activation of nociceptive afferents by mechanical, thermal, or chemical stimulus) the nervous system generates a pain response (based on interpretation of the meaning of the threat) and generates an output to remove or reduce the threat. This can involve responses that range from simple, stereotypical flexor withdrawal reflex to a complex and flexible adaptation involving multiple body segments. Pain **alerts** the individual to the threat of pain and **motivates** the individual to change behavior to reduce the threat. It is through the motor system that behavior is changed, in conjunction with autonomic (e.g., increased heart rate; decreased peripheral vascular resistance) and other changes, to remove the threat.

Early theories of stereotypical motor adaptation to pain were consistent with

this hypothesis—to increase muscle activity to limit motion [56], or inhibit agonist activity and facilitate antagonist activity during voluntary movement [43]. In both cases the objective is protection, but through predictable changes in muscle activation. Although logical and supported by some evidence, the complexity of the human body means that changes in pain are rarely stereotypical [31]. For instance, when back pain is simulated by noxious stimulation to the back muscles, there is profound interindividual variation; although almost all individuals had a net increase in muscle activity and estimated spine stability, the change in pattern of muscle activity to achieve this varied [26]. More recent theories aim to account for variation observed experimentally and clinically [30,31,50]. These theories propose that the adaptation pain (1) changes motor function across a spectrum of alternatives from subtle redistribution of activity within or between muscles, to complete avoidance of movement, activity, or participation; (2) varies between individuals and tasks; (3) serves the overall aim, at least in the short term, to protect the painful or threatened body part from actual or anticipated pain or injury and has “real” or perceived short-term benefit; (4) has potential long-term consequences if it is maintained, excessive, or inappropriate; and (5) has multiple potential mechanisms at various levels of the nervous system that are influenced by biological, psychological, and social aspects of pain [30,31].

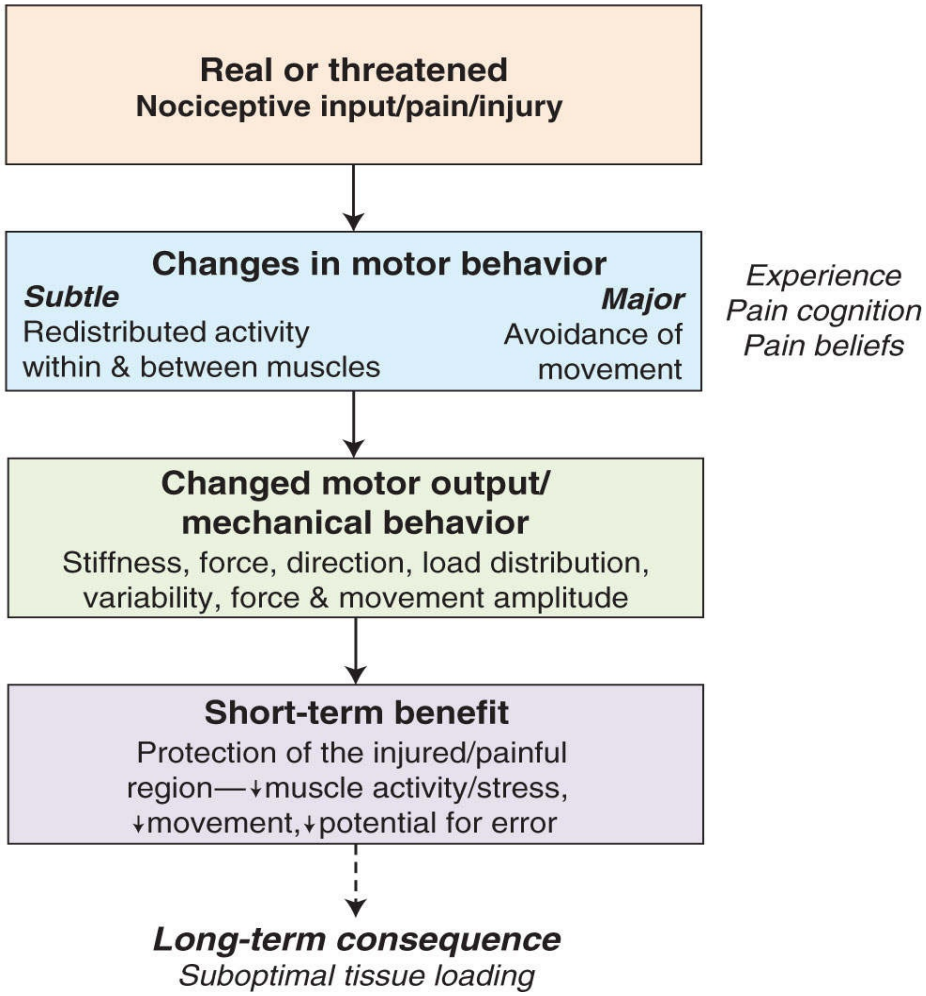

FIGURE 4-4 Protective response hypothesis. The logical response to pain and/or injury (or the threat of pain and/or injury) is to protect the injured/painful/threatened body region. This adaptation varies between individuals and tasks and can take many forms. Although logical in the short term, if sustained, the protective response can lead to further pain and injury of the same body region or other regions (e.g., adjacent joints) as a result of suboptimal loading.

Protection of the injured/painful/threatened body region may be achieved by many different responses. These could include (but are not limited to) increased stiffness to limit movement (e.g., splinting back muscles to limit spine movement [39]); decreased force amplitude (e.g., limping to limit force applied to injured ankle); changed force direction (e.g., change in direction of knee extension force to modify pressure on infra-patellar fat pad [71]); redistribution of activity within [70] and between [34] muscles to reduce muscle stress; avoidance of movement or function (e.g., bed rest); or avoidance of participation (e.g., work absenteeism). The specific solutions selected by the nervous system

to reduce threat will depend on many features that may vary between individuals and may not be constant within individuals. Factors that could influence the selection motor adaptation include the body region affected, the biomechanical options available to enable adaptation but maintain completion of the task, neuromuscular options available for adaptation (e.g., it may not be possible to redistribute activity between muscles in all contexts [35]), cognitive-emotional/psychosocial features (e.g., perceived consequences of unsuccessful adaptation; prior experience), or external demands (e.g., motivation to maintain behavior such as completion of a marathon).

In general it is assumed that some adaptations will be stereotypical and triggered with short latency from the exposure to threat (e.g., flexion withdrawal reflex [78]), but some will be learned over time (Bergin et al., unpublished data, 2015). Through trial and error, movement will adapt to “find” a solution that is less provocative or less injurious. Trial-to-trial variation in movement performance may subserve this search. Although some data show increased variation during pain [45,48], this is not universal [4] and different individuals may resolve to a new solution in different ways (Bergin et al., unpublished data, 2015).

Recognizing that the response to protect the tissues may also be linked to threat, anticipation, or fear is also important. In this case an individual may adopt a protective solution when one is not needed (fear of injury/pain when there is no real threat to the tissues) or a protective solution that exceeds that required to protect the tissues. A large literature related to fear avoidance (e.g., references [74,76]) that interleaves with this aspect of the interaction between pain/injury and motor control exists. In this context protective adaptation in terms of avoidance of activity or participation may be prevalent.

Although there is clear short-term advantage to adaptation, there may be long-term consequences [31]. Although the adapted motor behavior may reduce the actual or perceived threat to the tissues, it may also abnormally load the tissues of that or other body regions. If maintained, this could lead to further/additional problems. For instance, later relaxation of abdominal muscle activation after release of a load from the trunk (which could be interpreted to represent greater protection) is related to greater risk of a new back pain episode [8], and longer duration of co-contraction of medial knee muscles during gait in knee osteoarthritis is related to more rapid cartilage loss over time [32]. Thus, the *protective response* may underpin *suboptimal loading*, which leads to further pain of the affected or other body regions. In this case threat to the tissues was the motivator to change behavior in the first instance. If the protective response is maintained *beyond* when it is necessary, is in *excess* of what is necessary, or is

inappropriate, then resolution of symptoms may require reduction/removal of the protective response.

Conditioned Response Hypothesis

Recent emphasis has been placed on a fourth aspect of the relationship between movement/motor control and pain, which argues that an individual with pain may learn to associate movement with pain via a process of classical conditioning (Fig. 4-5) [49], in which movement produces pain by way of a learned association, without the requirement for ongoing nociceptor discharge from the tissues. This has also been referred to in terms of pain "memories" [51]. The process of association of pain with movement is thought to occur via process identical to that which induced Pavlov's dog to salivate (conditioned response) in response to ringing of a bell (conditioned stimulus) after it had been presented concurrently with the smell of meat (unconditioned stimulus) [55]. Movement may initially be provocative of symptoms because of nociceptor activation due to tissue loading (with or without sensitization). Over time, via a process of classical conditioning, pain (the conditioned response) may be experienced in association with movement (the conditioned stimulus), in the absence of nociceptive discharge (the unconditioned stimulus). An individual may continue to experience pain with movement, in the absence of input from the peripheral tissues and may continue to use or even enhance an adapted motor behavior (see section "Protective Response Hypothesis" above). Some evidence for the association of movement with pain (e.g., when individuals with neck pain are provided feedback that indicates more movement than is actually performed, pain is experienced earlier in the actual range [23]) exists. Treatment in the case of conditioning would require attempts to extinguish the association between movement and pain.

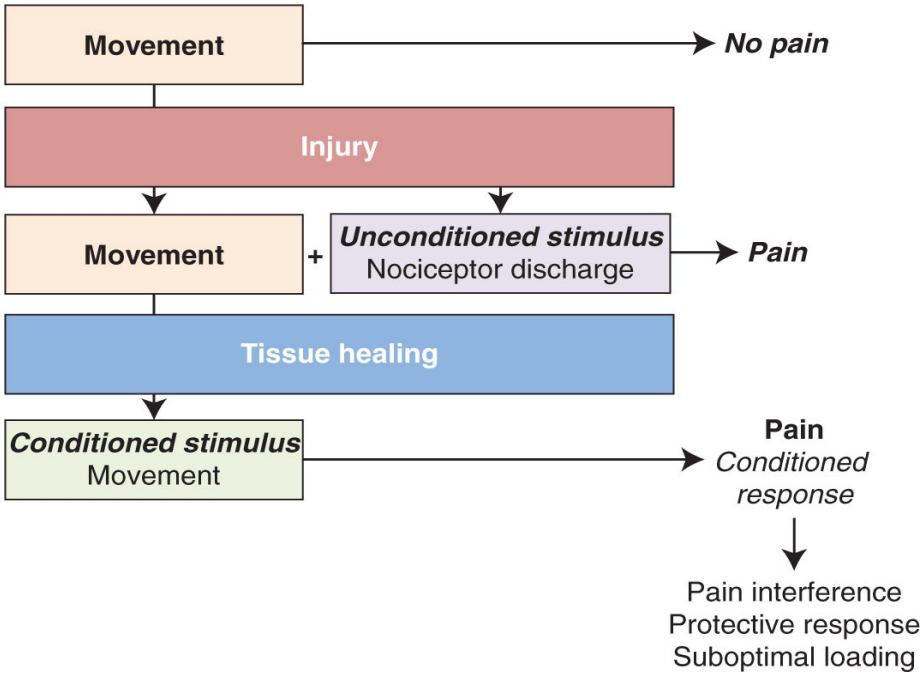

FIGURE 4-5 Conditioned response hypothesis. Via a process of classical conditioning repeated, simultaneous exposure of an individual to movement and pain (initially from nociceptor input) can lead to the movement being experienced as painful, despite the absence of nociceptor activation. This can lead to pain interference and protective responses, despite the absence of actual threat to the tissues from the movement.

Integration of Hypotheses

The four hypotheses to explain the interaction between pain/injury and motor control are not mutually exclusive; in fact, it is likely that the changes in motor control identified in association with pain/injury can only be understood by considering the interaction between these options (Fig. 4-1). It is likely that all coexist, but explain different aspects of the change in motor control in the presence of pain. The mix of mechanisms active in an individual will vary, the manner in which they are expressed will vary, and this will most likely change over time. Each has clear implications for treatment, and the potential success of an intervention is likely to depend on identification of the mechanism underpinning the motor control change and finding a treatment to target it.

CONSIDERATION OF MOTOR CONTROL IN THE TREATMENT OF PEOPLE IN PAIN

Different mechanisms will require different treatments. Some basic concepts are as follows:

1. If motor strategy leads to *suboptimal loading* of tissues, then training the individual to change strategy to a more optimal solution to load tissues in a healthy manner may be helpful.
2. If pain and/or injury *interfere* with movement, then treatments that target the interference and counteract the effects/consequences of interference are likely to be required.
3. If a *protective* motor adaptation is greater than is necessary or sustained beyond the time that it is necessary with subsequent suboptimal loading of the tissues, then training is likely to be required to resolve/reduce the motor adaptation to load the tissues in a more healthy manner and to restore activity and participation.
4. If movement is *conditioned* to induce pain, then interventions to extinguish the conditioning would be required.

Treatment of an individual is likely to require consideration of a combination of the concepts. Each requires further brief consideration.

Options to Train Optimal Loading and Resolve Excessive Protection

If suboptimal loading of tissues (as a *precursor to pain/injury* or secondary to a *protective reaction* or *pain/injury interference*) continues to contribute to the persistence of symptoms or contributes to development of related secondary changes (e.g., new problems in adjacent body regions), treatment strategies to retrain motor control may be required. Multiple treatment options may be available. Options include “skill learning” or “motor relearning” to specifically target the feature of motor control that is considered to underpin the suboptimal loading [33], generic training that aims to change motor function without specific attention to individual features [7], or strategies to automatically modify motor function [6].

Motor learning that targets specific features of motor control require detailed assessment of an individual’s motor control and development of a clinical rationale for the relationship to symptom behavior. In general the approach proceeds with cognitive modification of a movement, posture/alignment, or muscle activation strategy, followed by practice in a range of environments to

ensure integration of the new solution in function, utilizing motor learning principles [18,20]. This process can be facilitated by identification of clinical subgroups of patients that can assist with prioritization of treatment [40,53]. Multiple programs have been described to train motor function in this manner for the back [33,52,57], neck [38], and peripheral joints [58].

Generic training program may aim to encourage adoption of movement strategies that are considered “healthy” without detailed specific attention to an individual presenting movement behavior. Although some clinicians apply these interventions in a more individualized manner, typical examples could be ball exercises, many Pilates programs, and generic core stability exercises.

Some clinical approaches to modification of movement strategies rely on techniques to “automatically” change motor control. A range of clinical techniques is common in clinical practice. These may include application of tape, manipulative therapy, dry-needling, and so forth. In many cases the results are variable and the efficacy is unclear.

Options to Target Interference and Counteract the Effects of Interference

Strategies to overcome interference are those that target the mechanisms of interference or its outcome. For instance, reflex inhibition is likely to be best managed by treatments that reduce the stimulus (e.g., reduce intra-articular swelling) and target activation of the muscle affected by inhibition to counteract atrophy [25] and so forth. Identification of the stimulus for the interference is likely to aid optimization of treatment efficacy. Stimuli could include maintained nociceptive and non-nociceptive afferent input, inflammation, and so forth.

Counteracting the effects of interference is unlikely to be achieved through generic strength training and is likely to require specific training to target a change in muscle activation pattern, alignment, or movement. Options to address interference can be targeted at any level of motor system. Interventions may be targeted at the muscle (activation, specific strength training), the spinal cord (facilitation/inhibition of excitability), and supraspinal features (e.g., somatosensory awareness, motor map). Options similar to those described above to counteract *suboptimal loading* are likely to apply.

Options to Extinguish Conditioning

If movement is conditioned to induce pain, treatment should aim to extinguish

the conditioning [51]. Experience with painfree movement is the crux of this approach. This might be achieved through exercise combined with pain neuroscience education [51], but may be enhanced by training with virtual movement, where movement is perceived without any actual movement [23]. Current work is underway by several groups to identify methods to optimize this approach.

Evidence of Efficacy

It is unlikely that the blanket application of any solution to people with pain will be effective, and outcome is likely to be optimized if *right treatment* targeted to the *right patient* at the *right time*. Features of motor control can be changed with treatment. This includes changes in posture [16], sensory function [36], and muscle activation in trials of neck pain [37], back pain [68], and knee pain [10]. Some evidence exists of a relationship between changes in motor control and changes in clinical symptoms. But not all data are supportive [77].

Considering that intervention that targets features of motor control are unlikely to be required or beneficial by all individuals with pain is critical. Most systematic reviews of treatment of musculoskeletal conditions show that exercise is effective, but with limited effect size [73]. Key issues with interpretation of the literature are that many clinical trials treat all individuals with a similar intervention, systematic reviews generally group interventions together despite vastly different mechanisms, and most clinical trials include individuals in a nonspecific manner. Few attempts have been made to match the right treatment to the right patient at the right time, and this is likely to be critical considering the complex mix of mechanisms that link pain/injury and motor control. Substantial work still remains to be done.

CONCLUSION

This chapter has outlined four different viewpoints that are necessary to consider the changes in motor control that present of pain and/or injury. These viewpoints are clearly interrelated and all are needed to explain different aspects of the changes in motor control that present in an individual. Each mechanism has implications for selection of treatment, and there is potential for gains in efficacy of interventions if this interaction can be understood such that the right treatment is applied to the right patient at the right time.

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CHAPTER 5

Individual Differences and Pain Variability

Laura A. Frey Law and Steve Z. George

Pain is both a diagnostic and a prognostic indicator. For example, knee pain may be the first indication of osteoarthritis. However, the experience of pain can vary considerably among individuals with osteoarthritis. For example, severity of knee pain and severity of osteoarthritic radiographic findings are not well correlated. Indeed, physical therapists commonly observe variability among individuals, finding that some patients are more or less sensitive to apparently similar pathology or painful stimuli. Individual differences in pain sensitivity result in variability in the pain experience at the group or population level. This chapter will explore selected clinically relevant factors that contribute to this interindividual variability.

Pain variability can be observed under clinical and experimental conditions, with each condition providing a unique perspective on the pain experience. Variability of pain in clinical pain conditions can be challenging to assess as it may be confounded by the duration of the disease process, the severity of the underlying injury, the effects of previous treatment, and the use of varying coping strategies. Experimental models provide a means to study standard nociceptive stimuli across individuals to better delineate factors that contribute to pain variability. These models also allow for assessment of different components of the pain experience that may or may not be readily available in clinical settings. Pain sensitivity can be evaluated in two basic ways: (1) applying a constant noxious stimulus across individuals to assess differences in pain response; and (2) applying varying levels of noxious stimuli to assess a given pain response (i.e., threshold, tolerance, or some other predefined pain response). Increasingly, quantitative sensory testing (QST) is used in both research and clinical environments to determine pain threshold, tolerance, and responses to standard stimuli across multiple nociceptive modalities. These assessments allow for group comparisons to be made, to compare individual responses with normative values, or to predict patient outcomes. The use of both experimental pain models in healthy subjects and QST in patient populations has

increased our understanding of the extent of, and factors contributing to, variability in pain sensitivity.

Specific examples of interindividual pain variability from experimental conditions can be seen in Fig. 5-1. Fig. 5-1 depicts pain sensitivity, using both a constant stimulus (panel A, acidic intramuscular infusion) and a variable stimulus (panel B, pressure pain threshold), in a cohort of healthy subjects. The wide range of responses using both models provides a clear indication of the variability of the pain experience, even under controlled circumstances involving healthy subjects.

As defined by the International Association for the Study of Pain (IASP), pain is an unpleasant sensory and emotional experience related to actual or potential tissue damage. Pain sensitivity may depend on a myriad of factors (Fig. 5-2). Accordingly, a single factor is unlikely to explain the total variance in pain sensitivity. Further, these factors—sex, race, genetics, and psychological factors—are likely to interact in complex ways, making simple conclusions on the specific effect of a particular factor challenging. In this chapter, we will highlight the current status of the research on pain variability, acknowledging the inherent intricacies of the subject. We will discuss several sources of interindividual pain variability, considering studies of both clinical and experimental pain. We will focus on factors that have relevance to most clinical situations involving physical therapy: men versus women, ethnicity or race; psychological factors, age-related considerations, and heritability or genetics.

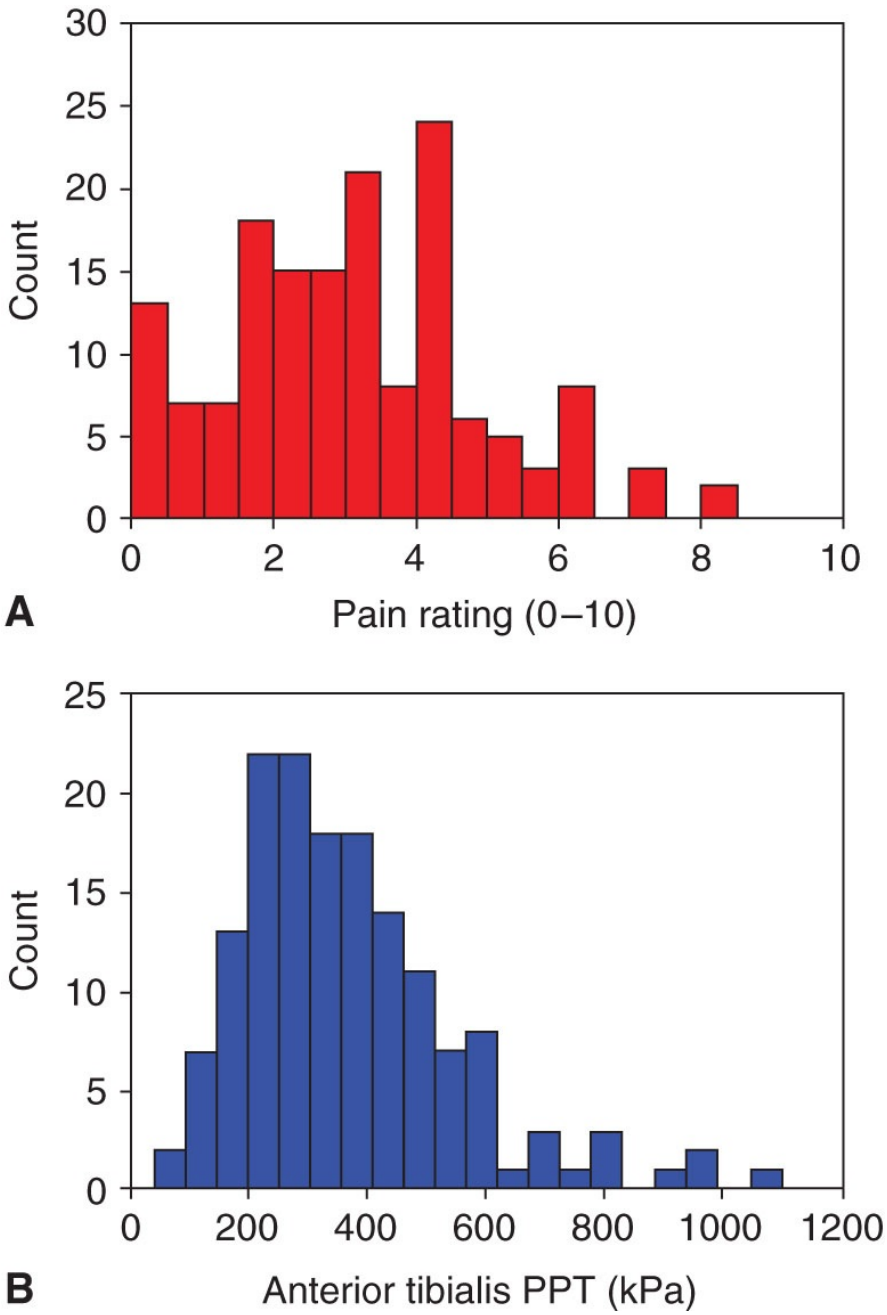

FIGURE 5-1 The distribution of **(A)** peak pain ratings (Borg CR10 scale) during intramuscular infusion of acidic phosphate buffer (pH 5.2) and **(B)** pressure pain thresholds (30 kPa/s) for 155 healthy subjects receiving these stimuli to the anterior tibialis (reanalyzed from Frey Law [20] and unpublished data). Both pain assessments showed nonnormal distributions and extensive variability with coefficients of variation (SD/mean) of 61.2% and 50.2% for panels **(A)** and **(B)**, respectively.

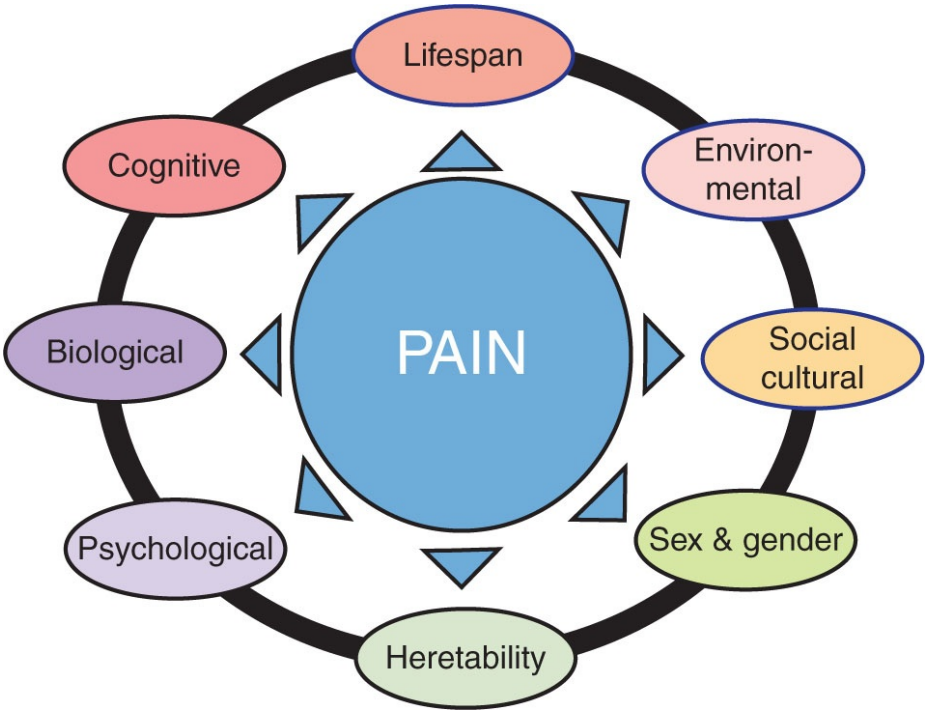

FIGURE 5-2 Schematic representation of multiple interacting factors that may influence an individual's perception of pain. (Modified and adapted from Berkley et al. [4] and Greenspan et al. [35].)

Pain sensitivity can be specific to the nature of the underlying stimulus; someone particularly sensitive to heat pain may not be sensitive to cold pain or deep-tissue pressure pain, and vice versa [38,43,56]. Additionally, pain sensitivity may depend on the nature of the measure; for example, pain threshold may vary considerably, whereas tolerance to the same pain stimulus may be relatively consistent across individuals or vice versa. Thus, caution should be used when considering which factors influence pain sensitivity—they may not generalize across all situations. Although one commonly hears a patient or his or her clinician indicate the patient has a "high" or "low" pain threshold or tolerance, this is an overly simplistic judgment. A therapist needs to understand that an individual is not likely to be equally sensitive to all possible noxious stimuli, and may be particularly sensitive to cold, pressure, or even exercise-induced pain, for example.

SEX AND GENDER

Although the terms *sex* and *gender* are often used interchangeably, we will define *sex* as the biological distinction between men and women, whereas

gender will be used to distinguish among social, cultural, or behavioral roles and expectations typically associated with men (e.g., masculinity) and women (e.g., femininity) [4,35,69]. Although sex and gender are frequently correlated, they are not synonyms. Our discussion will include both studies that have investigated sex differences and those that have taken into consideration the underlying gender roles. Sex is one of the easiest individual differences to classify, and more information is available on differences in pain between men and women than on differences related to gender role.

Sex Differences—Clinical Pain

Numerous clinical pain conditions are more prevalent in women, but some diagnoses are more frequently seen in men (see Tables 5-1 and 5-2) [3,35]. Several chronic musculoskeletal pain conditions commonly treated by physical therapists occur more frequently in women, such as: fibromyalgia, osteoarthritis (after age 45), temporomandibular joint disorder, and carpal tunnel syndrome [3,35]. However, not well understood is why these conditions may occur preferentially in women or whether women display greater pain sensitivity then men for similar diagnoses. In a review of multiple common recurrent pain conditions (headache, facial, back, musculoskeletal, and abdominal), women generally reported higher intensity, longer duration, and more frequent pains than men [82]. Similarly, women reported higher knee pain than men, after controlling for severity of radiographic knee osteoarthritis, particularly for the less severe (Kellgren–Lawrence grades <3) conditions [31]. However, in other studies, no sex differences in pain intensity were reported in chronic musculoskeletal pain conditions [22,68], but women reported a larger anatomical distribution of pain [22]. Further, no sex differences were noted in pain intensity ratings or medication use in cancer patients [81] or after oral surgery [43]. In fact, in a cohort of patients with acute and subacute low back pain, men reported higher pain intensity in comparison with women [23]. The mixed findings in observed clinical male–female differences may be related to differences in underlying pathology or tissue damage, peripherally or centrally mediated pain signal processing, or from biases in pain report or health care utilization. However, men and women use similar pain rating schemas [19], indicating that observed sex differences are not likely simply due to pain report bias. Thus, sex differences in clinical pain may be complex and vary by condition.

TABLE 5-1 Sex Prevalence of Various Painful Disorders

Female Prevalence	Male Prevalence	No Sex Prevalence
Migraine headache with aura	Migrane without aura	Acute tension headache
Chronic tension headache	Posttraumatic headache	"Jabs and jolts" syndrome
Postdural puncture headache	SUNCT syndrome	Secondary trigeminal neuralgia
Hemicrania continua	Raeder paratrigeminal syndrome	Neuralgia of nervus intermedius
Cervicogenic headache	Pancoast tumor	Painful ophthalmoplegia
Ticdouloureux	Thromboangiitis obliterans	Maxillary sinusitis
Temporomandibular joint disorder	Brachial plexus avulsion	Toothache due to dentinoenamel defects
Occipital neuralgia	Pancreatic disease	Toothache due to pulpitis
Periapical periodontitis and abscess	Duodenal ulcer	Cracked tooth syndrome
Atypical odontalgia	Abdominal migraine	Dry socket
Burning tongue	Lateral femoral cutaneous neuropathy	Vagus nerve neuralgia
Carotidynia	Postherpetic neuralgia	Stylohyoid process syndrome
Chronic paroxysmal hemicranias	Hemophilic arthropathy	Thoracic outlet syndrome
Temporal arteritis	Ankylosing spondylitis	Brachial plexus tumors
Carpal tunnel syndrome		Esophageal motility disorders
Raynaud disease		Chronic gastric ulcer
Chilblains		Crohn disease
Causalgia		Diverticular disease of colon
Reflex sympathetic dystrophy		Carcinoma of the colon
Hemicrania continua		Familial Mediterranean fever
Chronic venous insufficiency		Hereditary coproporphyria
Fibromyalgia syndrome		Acute herpes zoster
Esophagitis		Burns
Reflux esophagitis with peptic ulcer		
Slipping rib syndrome		
Twelfth rib syndrome		
Gallbladder disease		
Postcholecystectomy syndrome		
Irritable bowel syndrome		
Interstitial cystitis		
Acute intermittent porphyria		
Proctalgia fugax		
Chronic constipation		
Pyriformis syndrome		
Peroneal muscular atrophy		
Multiple sclerosis		
Rheumatoid arthritis		
Pain of psychological origin		

Abbreviation: SUNCT, short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing.
Source: Adapted from Greenspan et al. [35], with permission.

TABLE 5-2 Age-Dependent Sex Differences in Prevalence of Various Disorders

Female Prevalence	Male Prevalence
Gout (after age 60)	Gout (before age 60)
Osteoarthritis (after age 45)	Osteoarthritis (before age 45)
Livedo reticularis (after age 40)	Coronary artery disease (before age 65)
	Erythromelalgia (over age 50)

Source: Adapted from Greenspan et al. [35].

Sex Differences—Experimental Pain

Results from human studies using experimental pain models are also mixed when it comes to sex differences. Pressure or mechanical pain has shown the most consistent and largest effect sizes for male–female differences. In a meta-analysis of a total of 22 studies on sex differences to experimental stimuli, Riley et al. [64] found that women had lower pressure pain thresholds with a moderate effect size (Cohen's d = 0.59) and lower pressure pain tolerance with a large effect size (d = 1.18). Women also displayed lower thresholds for thermal pain (d = 0.46), electrical pain (d = 0.59), and ischemic pain (d = 0.18) [64]. Tolerance measures were also typically lower for women, but the effect size varied more between stimuli. The largest effect size was observed for pressure pain, but smaller effect sizes were observed for thermal pain (d = 0.09), electrical pain (d = 0.64), and ischemic pain (d = 0.16) [64]. More recently, Racine et al. [60] similarly concluded, from a meta-analysis of 122 publications, that sex differences are not consistent across multiple experimental pain modalities. However, both meta-analyses concurred that women exhibit greater sensitivity to thermal and pressure pain. Studies reporting pain ratings to a consistent algesic stimulus, such as pain with thermal probe at a set temperature, exercise-induced pain, or intramuscular infusions, have observed both elevated [20,40,43,44] and equal [10,20,41,43] pain responses in women compared with men.

It has been suggested that women may exhibit greater centrally mediated pain responses. Women have typically reported higher rates of temporal summation in response to thermal [18,29,70] and mechanical stimuli [72]. Temporal summation is the increased pain response to a consistent stimulus over time and is believed to be related to the central processing of pain at the spinal cord level. Higher rates of temporal summation are indicative of "amplification" of pain, and may be associated with the development of chronic pain syndromes. Referred pain and secondary mechanical hyperalgesia in the referred pain region, additional forms of centrally mediated pain, have also been observed more frequently in women than men [20,62]. However, no sex differences in secondary hyperalgesia have been noted with cutaneous heat and capsaicin pain models [41]. Collectively, these studies suggest that central processing of pain may differ between women and men, such that women have equal or higher pain sensitivity and may be at higher risk for the amplification of nociceptive signals.

Numerous studies have investigated the potential effect of the menstrual cycle in women on pain sensitivity. Contradictory reports reveal this issue is far from well understood. In one meta-analysis of 16 studies, women were least sensitive (i.e., had the highest thresholds) to pressure pain, cold pain, thermal

heat pain, and ischemic muscle pain during the follicular phase (days 6–11, immediately after the menstrual phase), with small to moderate effect sizes (Cohen's d = 0.34–0.48) [65]. However, in a subsequent review by Sherman and LeResche [73], the addition of different studies, coupled with inconsistencies in classifying menstrual phases in the prior studies, led to their conclusion that currently "little evidence" existed for menstrual cycle influences on experimentally evoked pain [73]. Similarly, in a recent review by Bartley and Fillingim [1], they acknowledge that studies in this area are limited by methodological weaknesses. Thus, future studies may still alter our understanding of the hormonal influences on pain sensitivity in women.

The experimental literature consistently suggests that women have equal or higher pain sensitivity than men, suggesting differences in peripheral sensitivity and central processing. However, the peripheral and centrally mediated sex differences may not be uniform across modalities or pain experiences. The studies outlined above, both clinical and experimental, do not account for gender or psychosocial factors, potentially important confounds.

Gender

Gender roles, which are influenced not only by the biological orientation of the individual, but also by social, cultural, and behavioral factors, have the potential to influence pain perception. Stereotypical gender roles suggest that men should have higher pain tolerance than women. This body of literature is much smaller than the previously reviewed literature related only to sex differences. However, there is some evidence to suggest gender influences pain perception, independent of biological orientation.

Measurement of gender roles is not as simple as determining biological orientation, but self-report questionnaires can be used. Several approaches to measure gender roles have been reported specifically in relation to pain, such as the Gender Roles Expectations of Pain (GREP), a measure that considers the influence of socially learned responses to pain for men and women [69], and the Extended Personal Attributes Questionnaire, which includes a measure of perceived masculinity/femininity. Others have assessed how strongly individuals associate with their ideal gender group [59]. In several experimental pain models, gender roles and expectations mediate observed sex differences. Willingness to report pain (on the GREP questionnaire) was found to be more meaningful than sex differences in explaining temporal summation [70]. This factor also added additional meaning to the sex differences in tolerance, threshold, and unpleasantness ratings to cold stimuli [90]. Similarly,

masculinity/femininity scores partially mediated the sex differences observed in a cold pressor task [79]. Participants with a strong gender group identity displayed large male–female differences for both hypothetical and electrically stimulated pain tolerance ratings, whereas men and women with low gender group identity reported similar tolerances [59]. Finally, when gender roles are manipulated, men and women have equal tolerance to cold stimuli [67], which suggests previously observed sex differences may be partially due to social expectations.

Bartley and Fillingim [1] indicated that psychosocial factors and coping strategies may differ between men and women, thereby contributing to sex differences in pain. This is supported by a subsequent study that found thermal pain threshold was greater in women [40], but largely explained by sex differences in ratings of pain-related fear (see section “Psychological Factors” later in this chapter). These various factors may be associated with gender roles, but have yet to be fully examined.

Gender roles have not been well explored in clinical settings. Women are more likely to seek medical attention and report health care complaints [50], although these results could spring from either sex or gender differences. However, a large cross-cultural study of multiple health complaints in adolescents suggests social gender roles could be contributing to these differences because they varied considerably between cultures [80]. The sex differences in recurring health complaints were generally small in 11-year-olds, but increased substantially by age 15 in some countries. This finding may be due to physiological changes with maturation, but may also be evidence for increased influence of social roles and expectations. In summary, although gender roles are likely to influence clinical pain, the relationship is not well understood.

ETHNICITY AND RACE

The terms *ethnicity* and *race* are often used interchangeably. However, for the purposes of this chapter, we will define *ethnicity* as belonging to a group of people who share a common background related to social, cultural, language, and geographical factors [61]. In contrast, the term *race* will be used to describe group membership on the basis of physical differences, although a strong social contribution to determination of race is acknowledged [47]. For example, the National Institutes of Health considers Caucasian, African American, and Asian

to be races, whereas Hispanic is considered an ethnicity. Similarly to sex and gender, both race and ethnicity can be confounded by additional complex social and cultural roles and expectations. Determination of ethnicity and race most commonly relies on subject self-report, and our discussion will focus on such studies that used this methodology for identification, as opposed to genetic definitions using ancestry markers. Next to sex, ethnicity and race are probably one of the most common differences identified during clinical encounters.

Clinical Pain

Several studies have reported on ethnic and racial differences in the clinical pain experience, with varied results. For example, migraine headache is more prevalent in Caucasians than in either African Americans or Asians; however, African Americans report higher migraine pain intensities [76]. African Americans generally report greater pain than Caucasians across the life span and across various patient populations [14,34], but inconsistencies are also observed. African Americans, compared with Caucasians, report greater pain with temporomandibular disorders [88], greater pain after surgery to correct scoliosis [87], and higher pain with lower experimental pain tolerance with chronic pain conditions [14]. Native Americans also have a higher prevalence of chronic pain compared with non-Hispanic White Americans overall in a review of 12 studies [42]. But this racial group has not been well studied historically.

Further complicating the issue, racial/ethnic associations with affective pain and disability ratings may differ from sensory–discriminative pain intensity ratings. For example, although African American subjects reported higher pain intensity from migraine headaches, their reports of pain disability were lower when compared with Caucasian subjects [76]. In another study, African Americans reported higher levels of pain unpleasantness, emotional distress, and pain behavior, despite similar pain intensities [66].

The inconsistency in these results may be due to other confounding factors such as sex, socioeconomic status, or pain location. When study participants are matched by sex, educational level, work status, duration of pain, and location of pain, similar levels of pain intensity, unpleasantness, and interference with activities are noted across the racial and ethnic groups [16]. However, higher pain intensity occurs in African Americans even when investigators control for age and socioeconomic status [76]. Overall, racial disparities in pain reporting as well as in pain treatment have been consistently documented [34]. Accordingly, Green et al. [34] suggest that greater education and training in racial and ethnic factors is warranted for all health care professionals.

Experimental Pain

The difficulty in comparing clinical pain conditions between ethnic and racial groups has led to interest in determining experimental pain sensitivities in both healthy and pain populations [6]. In a small sample of healthy college students, African American subjects had lower tolerance and higher ratings of unpleasantness to heat stimuli [15]. In a larger sample of college students, African American subjects had lower tolerance to heat, cold pressor and ischemic pain when compared with Caucasians [6]. However, only for heat stimuli were the differences in pain intensity and unpleasantness ratings significantly higher for African Americans [6]. These results were largely supported in a follow-up study, with Hispanic subjects also exhibiting lower tolerance to heat and cold when compared with non-Hispanic Caucasian subjects [61]. Although relatively little information is available involving additional races, African Americans, Hispanic and Asian Americans all had shorter withdrawal times and higher pain ratings than European Americans during the cold pressor task [43]. However, in a heat pain task, only Asian Americans displayed greater pain ratings at each temperature tested compared with African Americans, European Americans, and Hispanics [43].

Racial and ethnic differences may be more pronounced for experimental pain assessments than observed in clinical pain conditions. This statement is supported by an interesting study combining experimental and clinical pain models in patients seeking treatment for chronic pain conditions. Although African Americans reported both higher clinical pain intensity and disability ratings and lower experimental pain tolerance [14], the differences in clinical pain were smaller than the differences in experimental pain tolerance. Further, QST measurements and clinical pain reports in patients with knee osteoarthritis both showed greater pain and pain sensitivity in African Americans than in non-Hispanic Whites [9]. However, after controlling for education and annual income, the clinical pain racial differences diminished, but the QST pain sensitivity differences remained. This finding suggests larger racial differences with experimentally induced pain as compared with clinical pain.

In addition to experimental pain sensitivity studies, racial and ethnic differences in endogenous pain inhibition have been reported. Diffuse noxious inhibitory control (DNIC, see Chapter 3) represents an endogenous descending inhibition system, in which the application of a painful conditioning stimulus evokes a generalized analgesia, inhibiting pain from a noxious test stimulus. This phenomenon is also referred to as “pain inhibits pain.” Using a DNIC

protocol, one study found that non-Hispanic Caucasians had greater reduction in electrically induced pain following ischemic pain, when compared with African Americans, suggesting Caucasians may have greater descending pain inhibition than African Americans [7].

PSYCHOLOGICAL FACTORS

Negative Emotionality, Pain Catastrophizing, and Fear of Pain

Various approaches have been used to investigate psychological traits (enduring dimensions of psychological individual differences) and states (temporary or transient dimensions of psychological individual differences). Trait individual differences can be classified in many ways, but hierarchical structures have been increasingly recognized. These include traditional higher-order personality dimensions, such as neuroticism and extraversion; trait and mood scales, such as negative and positive affect or trait anxiety; and various dispositional or vulnerability scales, such as pain catastrophizing or pain-related fear. This section will focus on what we believe to be of most relevance for pain-related constructs—personality traits, negative emotionality, pain catastrophizing, and pain-related fear.

Personality traits have been characterized using several models, but the two most consistently described traits are neuroticism (also referred to as negative emotionality) and extraversion. Neuroticism is associated with anxious, worrisome, overly emotional, moody, and negative thoughts, feelings, and behaviors. Extraversion is associated with sociable, optimistic, excitement-craving, and easygoing traits. Neuroticism and extraversion are highly correlated with negative and positive affect, respectively; however, they are not opposites of each other [84]. For example, individuals can be high in both neuroticism and extraversion. Many personality assessment instruments are available, ranging from the100-item Eysenck Personality Questionnaire (EPQ) to the 10-item Positive and Negative Affect Schedule (PANAS) [84].

Pain catastrophizing is a negative cognitive style, which at the extreme includes feelings and beliefs that the pain experienced is beyond the control of the individual and will inevitably result in the worst possible outcome. Pain catastrophizing is believed to be a multidimensional construct comprised of magnification, rumination, and helplessness or pessimism. The Pain Catastrophizing Scale (PCS) is one example of a measure of pain catastrophizing

[77]. Example statements include: “I feel I can’t go on, it’s awful and I feel that it overwhelms me, and I anxiously want the pain to go away.” Another commonly used instrument is the Catastrophizing Scale of the Coping Strategies Questionnaire (CSQ) [71].

Pain-related fear can also be measured in multiple ways. The Fear of Pain Questionnaire-III (FPQ) is a self-report measure of anticipated fear for hypothetical situations that assesses severe pain (e.g., “breaking your neck”), minor pain (e.g., “having a muscle cramp”), and medical or procedure-related pain (e.g., “having a tooth pulled”) [52]. A high score on the FPQ indicates a high level of pain-related fear. The Fear-Avoidance Beliefs Questionnaire (FABQ) assesses pain-related fear associated with clinical pain conditions, specifically addressing fear-avoidance beliefs of physical activity [83]. A practical example is an individual with an elevated FABQ score would be hesitant to resume therapeutic exercise in response to shoulder pain, believing such activity would result in reinjury. Pain-related fear may depend on an individual’s prior pain experiences, present stress level, pain behavior, and certain personality traits.

Clinical Pain

Negative emotionality and its related subfacets have been associated with chronic pain perception, such that patients who express greater negative emotionality are more likely to report more health complaints and chronic pain conditions [32,53,85]. Similarly, pain catastrophizing and pain-related fear are associated with poorer function and greater pain in patient populations, such as those with osteoarthritis [75], shoulder pain [28], or fibromyalgia [33,37]. However, these cross-sectional studies are unable to clarify whether the poor health and chronic pain led to greater negative affect or vice versa.

Additional prospective research suggests pain-related fear and catastrophizing can predict greater pain and poorer outcomes in patient populations. Preoperative pain catastrophizing was the best predictor of poor self-reported function 6 months after total knee replacement in a prospective study of 140 patients [63]. Patients with elevated pain-related fear and catastrophizing measures at the acute stage of low back pain were more likely to have greater disability for up to 6 months [25,58], and at 1 year [5]. However, elevated pain-related fear (as measured on the FABQ) was predictive of work status at 1 year when examined in isolation, but only pain centralization was predictive when several factors were considered simultaneously [86]. Finally, changes in pain catastrophizing were predictive of subsequent changes in pain in

57 patients with fibromyalgia [8], but not vice versa, suggesting the psychological factor preceded the change in pain. Collectively, these studies suggest a temporal relationship such that pain-related fear and pain catastrophizing at symptom onset are precursors of reports of greater pain and disability even 6–12 months later. Thus, they may be viewed as predictors of poor outcome and should be considered when looking at risk factors for chronicity.

Experimental Pain

A large body of literature has compared psychosocial individual differences in relation to experimental cutaneous pain. Higher self-reports of negative emotionality, anxiety, pain catastrophizing, and fear of pain are associated with lower pain thresholds, lower pain tolerance, and higher pain sensory and affective ratings [13,36]. For example, using the cold pressor task, fear of pain was a unique predictor of pain tolerance and intensity [23,39], whereas in another study only pain quality was predicted by pain-related fear and catastrophizing [48]. In patients with low back pain, fear avoidance was related to initial heat pain ratings, whereas catastrophizing was related to temporal summation, that is, the increase in pain ratings when the heat was maintained [29]. Fig. 5.3 shows an example of the association between fear of pain and heat pain ratings in an experimental pain condition. Higher pain ratings were positivity correlated with FPQ scores when a 49°C thermal stimulus was applied to the trunk in healthy individuals (S. George, unpublished data).

Although few studies exist involving experimental deep-tissue pain, temporomandibular muscle pain responses were partially explained by negative affect during hypertonic saline infusion [91]. Further, fear of pain and pain catastrophizing are predictive of pain intensity, evoked pain, development of kinesophobia, and shoulder disability in studies using the delayed onset muscle soreness (DOMS) model [26,27,57]. Similarly, using an intramuscular infusion model of pain, individuals with the highest negative emotionality traits reported greater primary pain, greater mechanical hyperalgesia, and were twice as likely to experience referred pain than those with low negative emotionality traits [49].

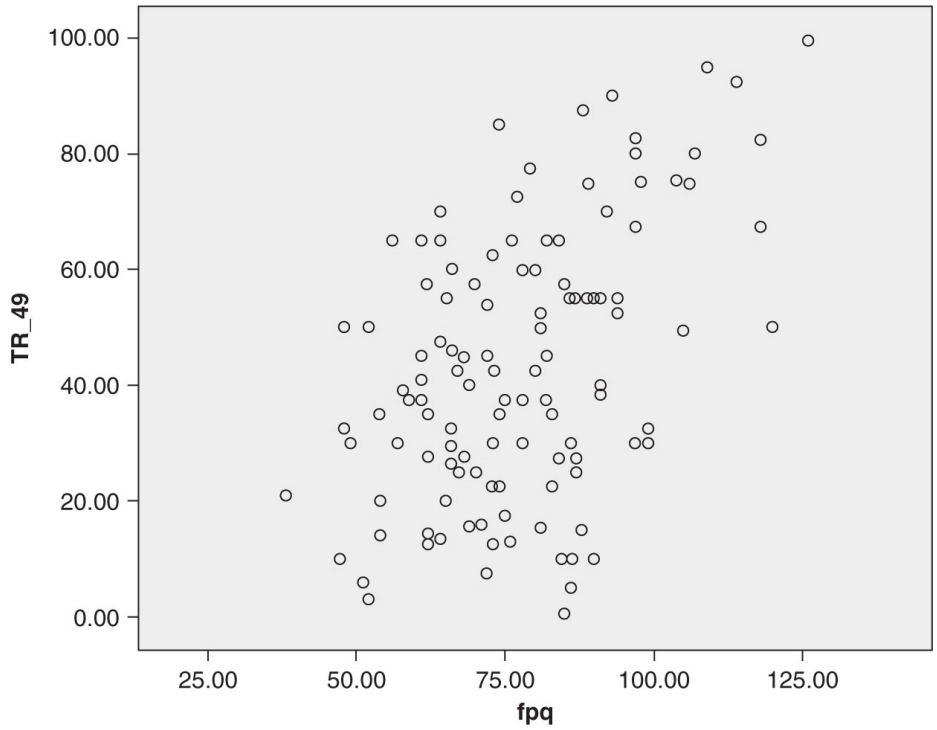

FIGURE 5-3 Fear of pain is associated with numerical experimental pain ratings on a scale of 0–100 (r = 0.47, $P < 0.01$) in response to 49°C stimuli to the trunk. Fear of pain was measured with the Fear of Pain Questionnaire-III (FPQ).

In summary, both clinical and experimental studies consistently support the association between pain or disability outcomes and negative temperament, pain catastrophizing, and pain-related fear. Furthermore, patients with low back pain differentially respond to rehabilitation on the basis of their fear-avoidance beliefs [21,24], suggesting patients' psychological traits may have important consequences on pain and disability and may affect the clinician's choice of treatment.

GENETICS AND HERITABILITY

The genetic influence on pain is challenging to study, in part because of difficulties in defining pain phenotypes. Sivert [74] defines a pain phenotype as "a measure that directly or indirectly reflects the processing of parts or the whole of the pain system, excluding tissue pathology and pain expression." However, tissue pathology is often a confounding factor in clinical pain phenotypes. The question arises, what constitutes a "pain gene"? Is a gene that is linked to osteoarthritis a pain gene or simply a gene linked to tissue pathology? There can

be several different pain phenotypes that may be impacted by a genetic factor, such as pain intensity, pain quality, pain duration, mechanical hyperalgesia, measures of centrally mediated pain facilitation or inhibition, or even response to pain treatment. Accordingly, the investigations of the genetic contributions to pain variability are still in their infancy and will likely continue to evolve.

Heritability has been traditionally investigated using twin studies (identical vs. fraternal twins) or family-based linkage studies to determine the underlying genetic versus environmental factors contributing to a disease. A recent meta-analysis of twin studies on clinical pain conditions reported estimates of 33–53% heritability for migraine and 30–38% heritability for back pain [55]. In clinical populations, it is challenging to differentiate the heritability of the underlying pathology as opposed to the heritability of experiencing pain. However, the authors specifically noted that one study, finding a common factor to explain nearly half the risk of developing pain at different musculoskeletal sites [89] and thus varied underlying pathological conditions, suggests that the genetic influence is likely to be primarily on pain processing. Although few twin studies have examined pain sensitivity specifically, one study involving experimentally evoked pain (cold pressor and thermal heat) demonstrated that genetics accounted for roughly 60% of the variance in cold pressor pain, but only 26% of the variance in heat pain [58].These twin studies collectively suggest that genetic factors can play an important role in pain sensitivity, but they may not influence different nociceptive stimuli or pain conditions equally.

Whereas twin studies have been used for some time to investigate the general heritability of various conditions, association studies investigating the links between specific genotype variations and pain phenotypes are increasingly common. The human genetic code was mapped only relatively recently, allowing researchers to examine single nucleotide polymorphisms (SNPs), that is, variations in the alleles G, C, T, A at a specific location on a gene. This advance has promoted rapidly evolving research on specific genetic variability as a contributing factor to various forms of pathology and disease. For example, 11% of the variance in a combined measure of overall pain sensitivity results from variations in a single gene [12].

Genetic influences on phenotypes can involve complex interactions between multiple genes and the environment. Accordingly, large sample sizes are typically needed to determine significant associations between genotype and pain phenotypes. To maximize statistical power and minimize false positives, multiple candidate pain genes have been identified and prioritized for use in association studies [2]. The criteria for prioritizing candidate pain genes for human association studies are: (1) adequate evidence supporting the gene’s role

in pain processing, (2) genetic variation frequent enough to affect clinical manifestation, and (3) a high likelihood that genetic variation affects protein function. Also gaining popularity are genome-wide association studies, which examine associations between phenotypes (e.g., pain) and SNPs sampled from across the entire human genome. Both approaches are likely to advance our understanding of the genetic influences on pain in the coming decades. Several lines of evidence now support the underlying hypothesis that genotype influences pain perception.

Three examples of high-priority genes that have been linked to pain perception in humans include the catecholamine-*o*-methyltransferase gene (*COMT*), the transient receptor potential subtype 1 gene (*TRPV1*), and the μ-opioid receptor gene (*OPRM1*). The *COMT* gene is important for the enzymatic breakdown of catecholamines—hormones released during physiological stress—such as epinephrine, norepinephrine, and dopamine. Thus, the *COMT* gene is likely involved in pain by altering the expression of the enzyme involved in the degradation of these substances. TRPV1, also known as the vanilloid receptor, is a membrane channel receptor found in both the peripheral and central nervous system. This receptor is activated by various nociceptive stimuli such as low pH, heat, and capsaicin (hot peppers), and is thus likely to be involved in pain transmission. OPRM1 is a μ-opioid receptor that is involved in the analgesic response to opioid drugs. The *OPRM1* gene is believed to be important in the variability of opioid response to medication and in the endogenous opioid mechanisms that serve to inhibit pain. These examples were selected only to highlight several genes that have been investigated in the literature, and are not meant to represent a systematic or comprehensive review of all pain-related genes.

Clinical Pain

Genetic studies involving clinical pain patients are only beginning to emerge. For example, in patients undergoing shoulder surgery, postsurgical pain at 3–5 months was associated with variations in the *COMT* gene with interactions with psychological traits [27]. The *GCH1* gene (which governs the expression of guanosine triphosphate cyclohydrolase I, an enzyme involved in catecholamine production) was associated with pain reports following diskectomy for radiculopathy [78]. As would be expected, the *OPRM1* gene was associated with the morphine (an opioid) dose needed for pain control in patients with cancer pain [46].

Experimental Pain

In healthy subjects, the *COMT* gene has been linked to pain perception and heterogeneity using thermal, mechanical, and ischemic experimental pain stimuli [11,12]. A study of muscle pain using the hypertonic saline model found that *COMT* was associated with cortical imaging of μ-opioid receptor binding, suggesting that this gene plays an important role in pain perception [91]. Additionally, the β-adrenergic receptors 2 and 3 genes (*ADRB2* and *ADRB3*) may also be important in mediating catecholamine levels, ultimately influencing pain sensitivity [54]. The *TRPV1* gene influences cold cutaneous pain, but not noxious heat in humans [44]. The *OPRM1* gene is associated with higher pressure pain thresholds [17] and with decreased event-related potentials from a pain stimulus [51] in healthy volunteers.

AGE

The effect of age on pain variability can be difficult to assess because several of the previously discussed factors (physiological, psychological, and social) may vary from youth through adulthood, and potentially on into older adult years. Although we have attempted to discuss several of these separately, considering them as a function of age has value for the clinician. A review of the literature including over 140 citations on age-related effects on pain concluded that thresholds were more frequently elevated (showing less sensitivity to pain) in older adults. However, the review found that age-related effects can vary with modality (thermal and mechanical more than electrical), location (distal more than proximal), and temporal/spatial characteristics [30]. It is less clear whether systematic changes in suprathreshold pain perception occur with aging. It is possible that older individuals may have a reduced region between pain awareness (threshold) and pain tolerance. Accordingly, advancing age may result in greater central sensitization, as determined by measures of temporal summation and secondary mechanical hyperalgesia, and less ability to endogenously inhibit pain, suggesting that older adults may experience greater pain sensitivity. Collectively, all of these changes result in nervous system adaptations that may delay initial onset of pain reports but take a longer time to resolve than younger adults [30].

COMPLEXITY

Each of the factors described above may interact in complex ways to influence pain. Although it is not yet clear how each of these interactions will ultimately affect diagnosis and treatment, it is important to realize these factors will influence a patient's perception of pain. Current clinical practice considers this complexity by using selected demographic, clinical, and psychological factors to determine risk profile for developing chronic pain. These factors are readily available and allow for reasonable accuracy in predicting outcomes. Typically, these factors are considered in isolation, which does not truly represent the complexity of the pain experience. However, recent studies have provided more complex risk assessment that allows clinicians to rate the relative risk of multiple factors. A recent manuscript highlights how this complexity may be used in phenotyping physical therapy patients with knee osteoarthritis [45]. These authors present a conceptual model considering knee pathology, psychological distress, and the neurobiology of pain that may be relevant to determining patient-specific, optimal therapeutic interventions. Accuracy of future risk profiles will be improved by simultaneously considering many of the factors discussed in this chapter to determine the expected response to pain.

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SECTION 2

Physical Therapy Pain Management

CHAPTER 6

Pain Assessment

Josimari M. DeSantana and Kathleen A. Sluka

GOALS OF PAIN ASSESSMENT

The goal of pain assessment is to provide sufficient and accurate data to determine what treatment should be initiated. Accurate pain assessment is the first step in effective pain management. Information must be obtained on the nature of the pain, physiologic, behavioral, and emotional responses, and previous experience with pain.

Pain is now considered the fifth vital sign by the American Pain Society and the Joint Commission (formerly known as the Joint Commission on Accreditation of Health Care Organizations regulations, which require that pain is assessed in all individuals [56]. This means the assessment of every patient for pain with every vital sign assessment. Assessment of pain is critical to understanding the nature of the pain as well as its meaning and impact on the individual. Proper assessment of pain is important to aid in diagnosis, to guide the choice of therapy, and to evaluate progress and effectiveness of therapy [56].

The Joint Commission does not specify a particular tool or scale to use, but does recommend that age appropriateness be considered when selecting a pain instrument. The United States Agency on Health Care Policy and Research (now the Agency on Health Care Research and Quality) guidelines also specify scheduled pain assessment/management and include specific infant recommendations [2]. Thus, pain should be routinely monitored, assessed, reassessed, and documented clearly to facilitate treatment and communication among health care clinicians [42].

Valid and reliable measurements of pain are needed to identify patients who require intervention and to evaluate the effectiveness of intervention. The two terms *pain assessment* and *pain measurement* are not interchangeable. They are widely used in the pain literature, but they have different meanings. Pain *assessment* connotes a more comprehensive and multifactorial concept,

describing a complex process in which information about pain, its meaning, and its effect on the person is considered along with quantitative values. Whereas, pain *measurement* connotes the quantification of various aspects of the pain experience, most commonly associated with the dimension of pain intensity [11,55,74].

This chapter will provide basic information about pain assessment and pain measurement; and review the types of subjective questions that can be evaluated to assess the nature of pain, specific instruments to measure pain, and measures that evaluate the impact of pain on the person and quality of life.

MEMORY FOR PAIN

Pain is commonly assessed with multiple questions about the worst pain, average pain, and least pain over the 24 hours or week or month. These questions are given because pain intensity normally fluctuates and varies over time, and thus a single pain intensity rating of current pain may not accurately reflect the pain experience. Common questions are such as “What is your pain at its worst in the last 24 hours?” or “What is your pain at the end of the day?” These questions imply that memory for pain is accurate or actual intensity of pain. Indeed short-term recall of pain intensity is accurate, particularly when one asks about average pain intensity over the last 24 hours or week [15,16,88]. In fact, there is strong agreement between the patients recalled usual pain intensity over a 7-day period and actual average pain intensities recorded over this period, but poor agreement between worst and least pain [15]. However, not surprisingly, long-term memory of pain intensity is less accurate (years later), whereas recall for activities reduced by pain is generally very good as is the recall for location of pain [30] (Fig. 6-1). As shown in Fig. 6-1A, people with low back pain (LBP) were asked to recall their average pain intensity at different times during the day or the least severe or most severe pain intensity. In this instance, people tended to overestimate their pain intensity when compared with measurements taken during the question. However, Fig. 6-1B and C show that pain location and activities affected by pain are easily recalled with accuracy. Thus, the use of short-term recall of usual pain intensity and location is an useful measure for gaining an understanding of the pain experience in people with acute and chronic pain. One might also add questions about activities affected by pain to the assessment.

The intensity of memory of pain is influenced by a number of factors,

including the intensity of the pain associated with a painful procedure. Patients' judgment of total pain correlates strongly with the peak intensity of pain but not with its duration [91]. There are distinct factors that determine the direction of pain memory: current pain intensity, emotion, expectation of pain, and peak intensity of previous pain [57]. Thus, it seems that the memory of pain is most strongly associated with pain intensity during the painful condition.

HISTORY OF PAIN

A thorough history to evaluate patients with pain includes an assessment of a number of variables that may play crucial roles in pain management. Patient's characteristics such as age, gender, and ethnicity should never be missed in the assessment. Also, it is important to evaluate the presence or absence of depression, and assess how pain is affecting patient's life, ratings of job satisfaction, and to describe the support system available at home and at work. Listed below are important considerations to evaluate regarding the history of pain:

1. Pattern, intensity, location, and duration of the current episode of pain;
2. How and when the pain starts;
3. Previous episodes of pain and its treatment;
4. Family history of similar pain condition;
5. Congenital problems since birth;
6. Exacerbating and relieving factors;
7. Condition of mood and appetite;
8. Quality of sleep;
9. Presence or absence of fatigue as well as its intensity;
10. Previous accidents or injuries involving that area with pain;
11. Activities during daily routine;
12. Work history;
13. Sports and other leisure activities;
14. History of cancer and other chronic illnesses;
15. Recent fever or unexplained weight loss;
16. Hormonal disturbance history;
17. Medication use, such as analgesics, anti-inflammatories, muscle relaxants, antidepressants, corticosteroids; and
18. Smoking and alcohol history.

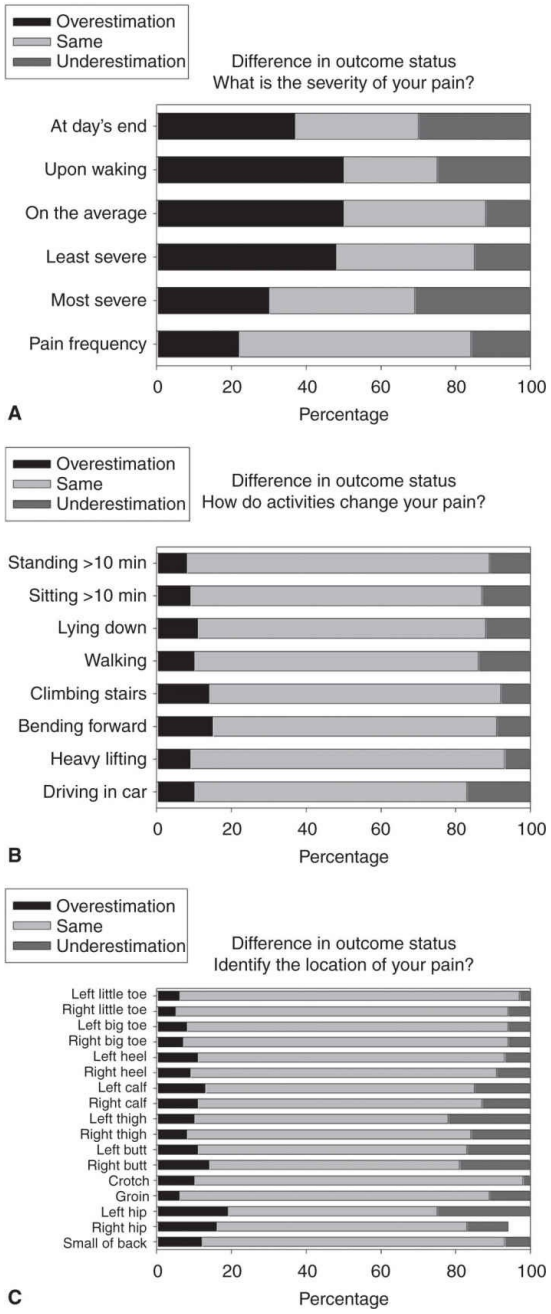


FIGURE 6-1 Graphs (A)–(C) show the likelihood that someone would overestimate, underestimate, or produce the same result for three different parameters related to pain: (A) intensity, (B) activities that affect pain, and (C) location of the pain. As can be seen there is a lot of variability when people are asked to remember the intensity of pain, but substantially less when asked what activities can change their pain or the location of the pain. (Reprinted with permission from Dawson et al. [30] [Figures 2, 4, and 5].)

TECHNIQUES FOR PAIN ASSESSMENT

Tools for pain measures must have well-established reliability and validity and should have been used previously to assess pain outcomes. The types of assessments used will vary depending on the nature of the pain (acute or chronic), and the practice setting of the therapist (private practice, hospital based, multidisciplinary unit). In acute pain, using the biomedical approach to pain assessment is frequently useful; however, it may not adequately assess the impact of pain on the person. However, in some acute pain situations and in chronic pain conditions, a more biopsychosocial approach to pain assessment will be required. Understanding the psychosocial constructs associated with acute pain will aid in recovery of acute pain and may prevent the transition from acute to chronic pain. For example, the impact of a severe ankle sprain may have a more significant impact on a construction worker whose livelihood depends on the ability to use the leg, than on an office worker who spends the majority of their day at work on a computer. Furthermore, several psychological factors (i.e., depression, anxiety, fear avoidance, and pain catastrophizing) are strong predictors of chronic pain after surgery, poor prognosis in both acute and chronic pain, and the transition from acute to chronic pain [20,51,63,83,90].

There are two main kinds of tools or scales for assessing pain: unidimensional and multidimensional. A unidimensional scale usually measures only one construct (e.g., pain intensity). A multidimensional scale simultaneously measures different constructs, whether or not it actually contains separate scales for each of these.

Pain measures are often classified as self-report, behavioral/observational, or physiological [113]. Self-report is the best method of assessing pain. Many validated self-report tools are available to help children and adults communicate their pain intensity. Patients unable to self-report pain must rely on others to recognize that they are in pain, assess the source of their pain, and then manage their pain accordingly.

Self-Report

Self-report measures are considered the “gold standard,” and the most valid approach to pain measurement. Although self-report measures exist in verbal and nonverbal formats, both require sufficient cognitive and language development to understand the task and generate an accurate response [13,74]. Verbal self-report measures include structured interviews, questionnaires, self-

rating scales, and pain adjective descriptors. Nonverbal measures include facial expression scales, visual analog scale (VAS), and drawings [13,74].

Using a global rating scale, the therapist provides a rate of a patient's pain intensity. Metric and tool such as numerical rating scales (NRSs), VASs, and faces scales have been utilized as the foundation for global observational rating scales [17,24,25,39,108,111].

Facial expression seems to have an important role in the measurement of pain [28]. Most behavioral checklists and rating scales include items referring to the face. Facial expression scales are often used with young children to obtain a self-report of pain. All consist of a series of faces with varying expressions that range from neutral or smiling to distress or crying. The response requirement for young children is to point to the face that corresponds most closely to how much pain they have (intensity) [10,12,48], how the pain makes them feel (affect) [70], or both [116]. Facial expression scales are easy to administer, and most of them demonstrate adequate to excellent psychometric properties.

Behavior/Observation

In the absence of self-report, observation of behavior is a valid approach to pain assessment. Pain behaviors do not always mirror the pain intensity accurately, and in some cases indicate another cause of distress, such as physiologic or emotional distress [87]. The circumstances of the behavior and its potential sources must be considered when determining pain management. Consciousness of individual baseline behaviors and changes that happen with discomfort are very useful in differentiating pain from other causes. A number of behavioral checklists and behavioral rating scales are available in the literature for assessing pain.

A behavior checklist provides a list of behaviors that are marked as either present (usually scored 1) or absent (usually scored 0) with no judgment of intensity or frequency of the behavior [13,23]. The pain intensity score is defined as the number of items checked. The most common behavioral indices of pain in these scales include vocal, verbal, facial, postural, and motor behaviors. The instrument may or may not require observation for a specific period of time. Pain intensity is assumed to be greater if the observer notes a greater number of overt displays of pain.

Behavior rating scales incorporate a rating of the intensity, frequency, or duration of each behavior [3,36,70]. The most frequently used rating for individual behaviors is 0 (absent) to 2 (intense or frequent), but many other metrics have been used. In some such instruments, the metric chosen for each

behavior may deliberately reflect the weight placed on that behavior as an index of pain; in other instruments, all items are arbitrarily weighted equally. Similarly, the number of items reflecting a particular domain of behavior may be chosen either on the basis of evidence-based weighting, or more commonly arbitrarily, or on the basis of the investigator's opinion. This approach allows for gradations in intensity or frequency of expressions of pain.

Observation of children's physical behaviors can be used to assess children's pain. These scales must be used to suppose pain in infants, children who are unable to communicate, children who are too young to comprehend the use of self-report scales, and children with cognitive impairment and/or physical handicaps. Numerous behavioral scales have been developed that measure crying, facial expressions, verbal communication, and body movement as indicators of pain and distress [73,101].

Physiological Parameters

Physiologic parameters such as heart rate, respiration rate, blood pressure, palmar sweating, cortisol levels, transcutaneous oxygen, vagal tone, and endorphin concentrations [29,105] have been tested as pain measures. Other physiologic responses to pain include pupil dilation, flushing or pallor, nausea, and decrease in oxygen saturation. However, physiological measures are not sensitive or specific as indicators of long-lasting pain and thus can only be used as supplementary to behavioral observations [37,106,117].

Physiologic changes are seen primarily in the early stage of acute pain and usually subside with prolonged or chronic pain because of adaptation, making them unreliable indicators of persistent pain. Physiologic responses in children match with their distress in a painful procedure or condition and mirror a global response to stress. There is not enough evidence to support any direct correlation between these physiologic responses and pain experience. Thus, they are not optimal measures of pain experience. However, many of these parameters have been incorporated into behavioral scales to form a more comprehensive assessment, mainly in infants and nonverbal children.

Physiological parameters cannot be interpreted as a sign of and pain in a number of situations because (1) pain is a stressor, and changes in physiological parameters can occur as a response to either noxious stimuli or stress; (2) those parameters have been used to investigate short-duration, sharp pain, and there is a habituation of physiological responses to long-term pain [74,103]. Thus, physiological parameters should be used as a complementary measure to other.

PAIN ASSESSMENT IN ADULTS

Multidimensional Pain Measurement

As we discussed in prior chapters, pain is a multidimensional experience that results in multiple impairments, functional limitations, and disabilities. As such, the measurement of pain should address not only the intensity of pain, but also the multidimensional nature of the pain experience as well as the impact on function and disability. Unidimensional scales have been successfully utilized in recording pain intensity, are quick and easy to use, and are responsive to treatment. However, for a more complex understanding of the pain experience, measurements need to assess the sensory and emotional components of pain, the impact of pain on the person, and potential psychological confounders. The following sections will provide several different pain measures aimed at addressing the multidimensional nature of pain and the impact of pain on the person.

Pain Scales

There are several pain rating scales available to assess pain intensity. These scales have the advantage of being easy and quick to use, quantifiable, valid, reliable, and useful. Further they are simple for the patient to understand and are sensitive to both pharmacological and nonpharmacological treatments. Pain rating scales such as VAS, NRS, and verbal rating scale have been commonly used to assess adult's pain in the clinical practice as well as clinical trials.

Using the **NRS**, individuals are asked to rate the intensity of pain on a scale of 0 (no pain) to 10 (worst pain). This scale is simple to administer, the results are easily recorded, and it gives the most information when used in the sequential evaluation of pain and response to pain relief interventions [64] (Fig. 6-2A).

The **VAS** consists of a 10-cm vertical or horizontal line, where the ends of the line represent the extreme limits of pain intensity (e.g., no pain or the worst pain imaginable) (Fig. 6-2B). Patients are asked to select a point or make a mark along the line to indicate the intensity of their pain. There are many versions of VASs found in the literature. Differences between them include the anchor terminology, the presence or absence of divisions along the line, the units of measurement (e.g., cm or mm), the length of the scale (i.e., 10, 20, or 100 cm), and whether the scale was presented as a vertical or a horizontal line [100]. The

VAS is easy to administrate and reproduce, and is applicable as a measure of pain in older children, adolescents, and adults [41].

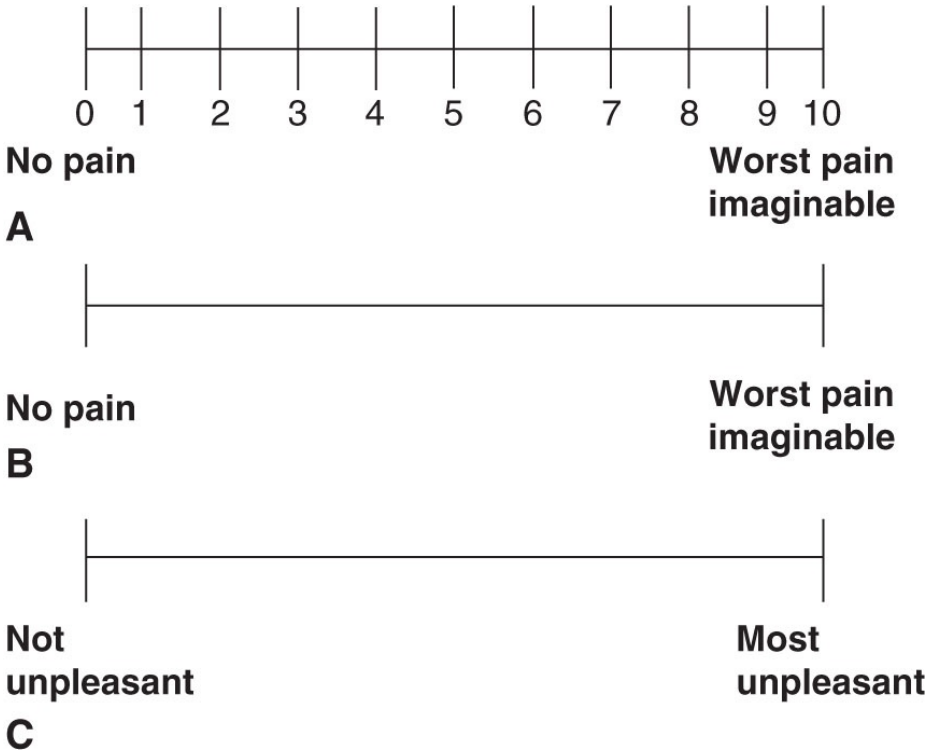


FIGURE 6-2 A: Numerical rating scale (NRS) for pain. B: Visual analog scale for pain intensity. C: Visual analog scale for pain unpleasantness.

Some authors, recognizing the difficulty in discriminating pain intensity from pain unpleasantness and from other emotions such as fear, have adopted less specific terms such as “distress” or even “quality of life” in place of “pain” in the title of their scale. Nevertheless, such scales may be treated by other researchers as predominantly or purely pain scales, and such “non-pain” scales are generally neither more nor less responsive to pain-producing or pain-relieving interventions than are scales explicitly labeled as measures of pain. Few researchers have presented discriminant validity data showing that their observational scales can differentiate pain intensity from its affective aspect or from other negative emotional states and reactions (Fig. 6-2C).

Body Diagrams

The use of a body diagram allows the patient to draw the location of their pain on a diagram. This is a simple way to gain a graphical representation of the location of a person’s pain. The therapist can simply ask the patient to draw the

location of their pain on the diagram [30] (Fig. 6-3). The body diagram also allows the therapist to determine if pain is localized to the body area they are seeking care for (i.e., low back) or if pain is more widespread. Understanding the widespread nature of pain complaints is important in understanding mechanisms (see Chapter 7) and understanding the impact of pain on the person. A survey of over 3000 individuals shows that in the last 7 days 23–38% of individuals were pain free and that for those with pain, only 15–18% had pain in one area [58]. In fact 23% of females and 11% of males had greater than five areas of pain. The significance of this relates to disability. Those with the most number of pain areas show the greatest difficulties with physical function, social activities, and mood, and the number of pain areas is directly proportional to the degree of disability (Fig. 6-4).

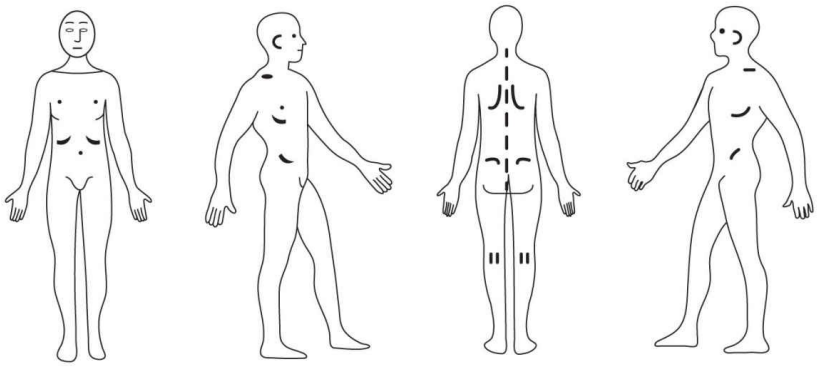


FIGURE 6-3 Example of a body diagram in which the subject can draw the location of their pain.

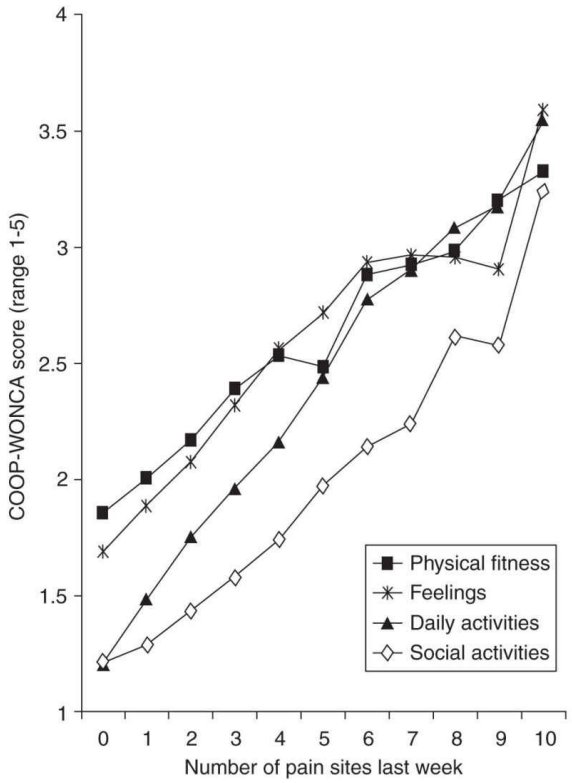


FIGURE 6-3 Example of a body diagram in which the subject can draw the location of their pain.

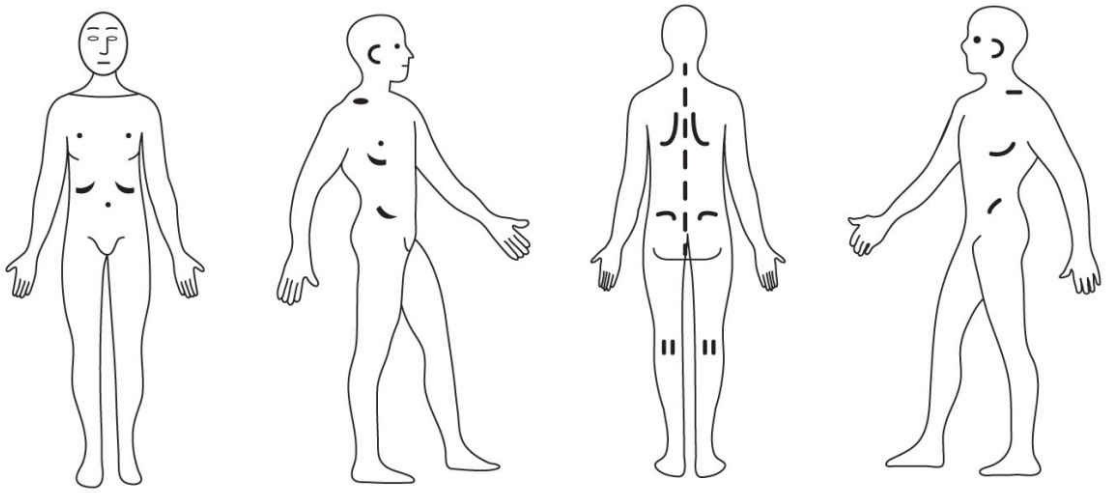


FIGURE 6-3 Example of a body diagram in which the subject can draw the location of their pain.

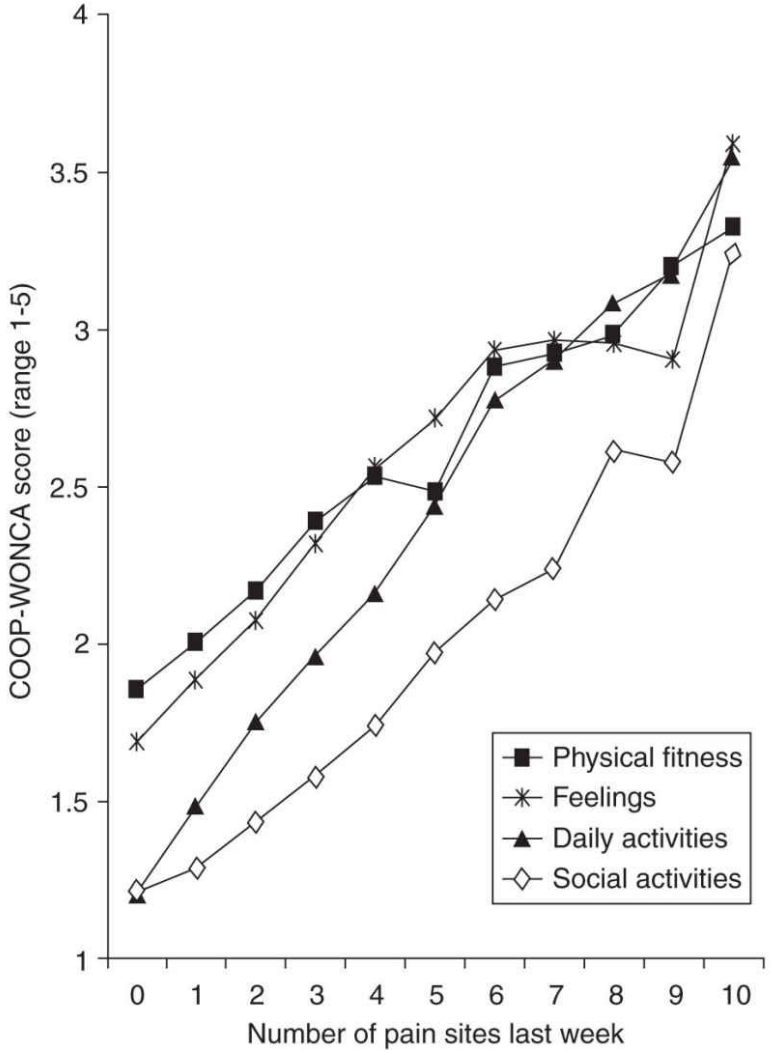


FIGURE 6-4 This graph shows patient responses to a disability questionnaire and how those responses correlate with the number of pain areas a person had in

the last week. Notice the linear relationship between more severe disability with the number of pain areas. (Reprinted from Kamaleri et al. [58] with permission from IASP.)

Pain Questionnaires

McGill Pain Questionnaire

Melzack and Casey [77] suggested that there are three major psychological dimensions of pain: sensory-discriminative, affective-motivational, and evaluative-cognitive. These three categories interact with one another to provide quantitative and qualitative information on the components of pain. These three dimensions formed the basis for the development of the McGill Pain Questionnaire (MPQ), which has been used as a tool for evaluating multidimensional aspects of the pain experience through the use of standard pain-related words. There is evidence that each pain condition is characterized by a distinctive group of words [96].

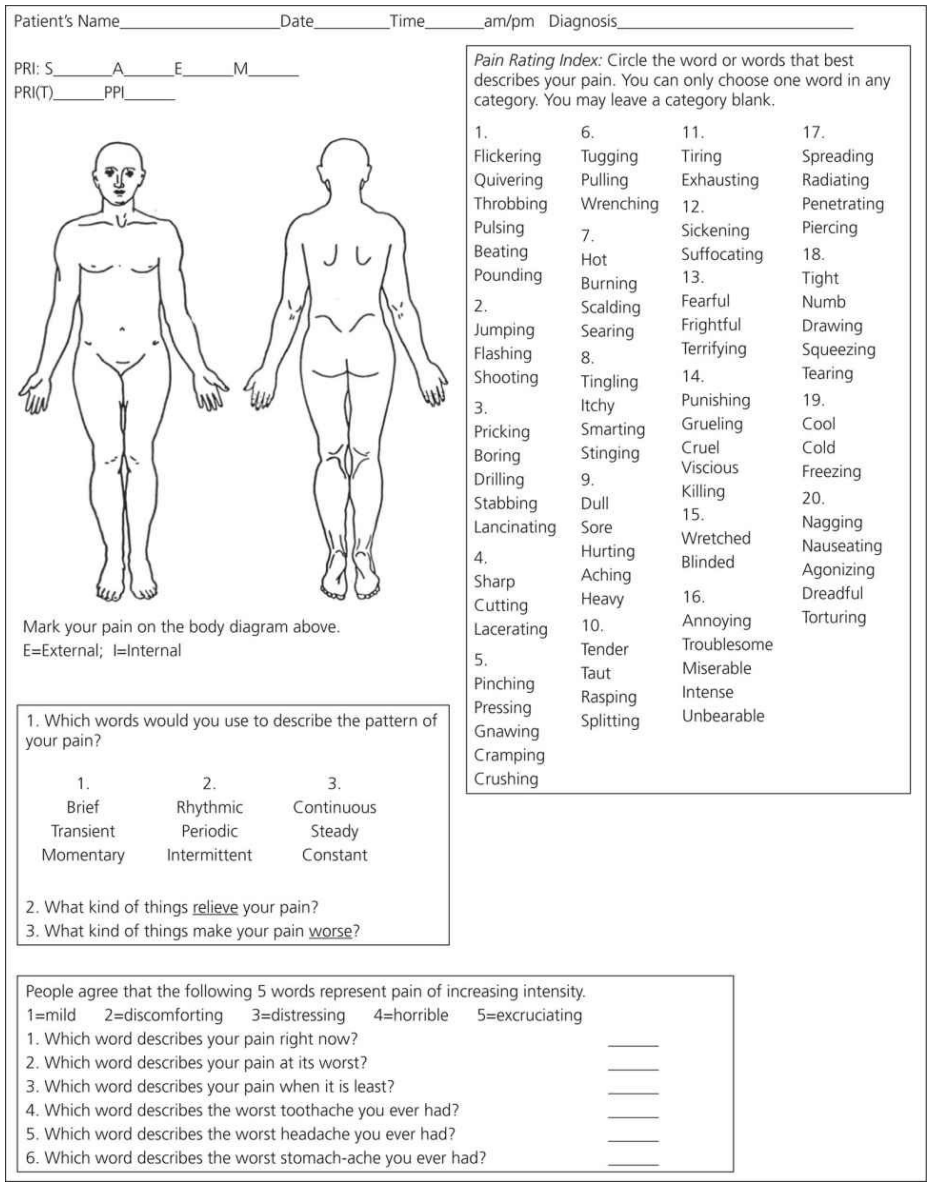


FIGURE 6-5 The original version of the McGill Pain Questionnaire (MPQ). The descriptors compose four major groups: sensory (S), 1–10; affective (A), 11–15; evaluative (E), 16; and miscellaneous (M), 17–20. The rank value for each descriptor is based on its position in the word set. The sum of the rank values is the pain rating index (PRI). The present pain intensity (PPI) is based on a scale of 0–5. (Reprinted with permission from Melzack [75].)

The MPQ offers a method to assess the sensory, affective, and evaluative components of pain. It is a self-administered measure consisting of four main parts [76] (Fig. 6-5). Firstly, patients draw the location of their current pain on a body diagram. In the second part, which is the major component of the questionnaire, there are 78 pain descriptors distributed across 20 subclasses,

which are classified in 5 supplementary classes. The subject is allowed to pick one, or no, words from each subclass. The *sensory* class contains 10 subclasses (1–10), the *affective* class includes 5 subclasses (11–15), the *evaluative* class has 1 (16), the *miscellaneous* class encompasses 5 (17–20), and the *total* class contains all categories from 1 to 20. Furthermore, each word from these categories has a rank value indicative of the relative intensity of pain. The third part measures how the pain changes over time and the parameters that relieve or increase it. As a final point, the fourth part has a single measure of pain intensity that ranges from 1 to 5.

Different scores can be obtained from the MPQ, such as the Number of Words Chosen (in part 2, range of 0–20), and the Present Pain Intensity (PPI) (in part 4, range of 1 [mild] to 5 [excruciating]). The rank values of the words chosen can be added to obtain a Pain Rating Index for each category as well as a total score [64].

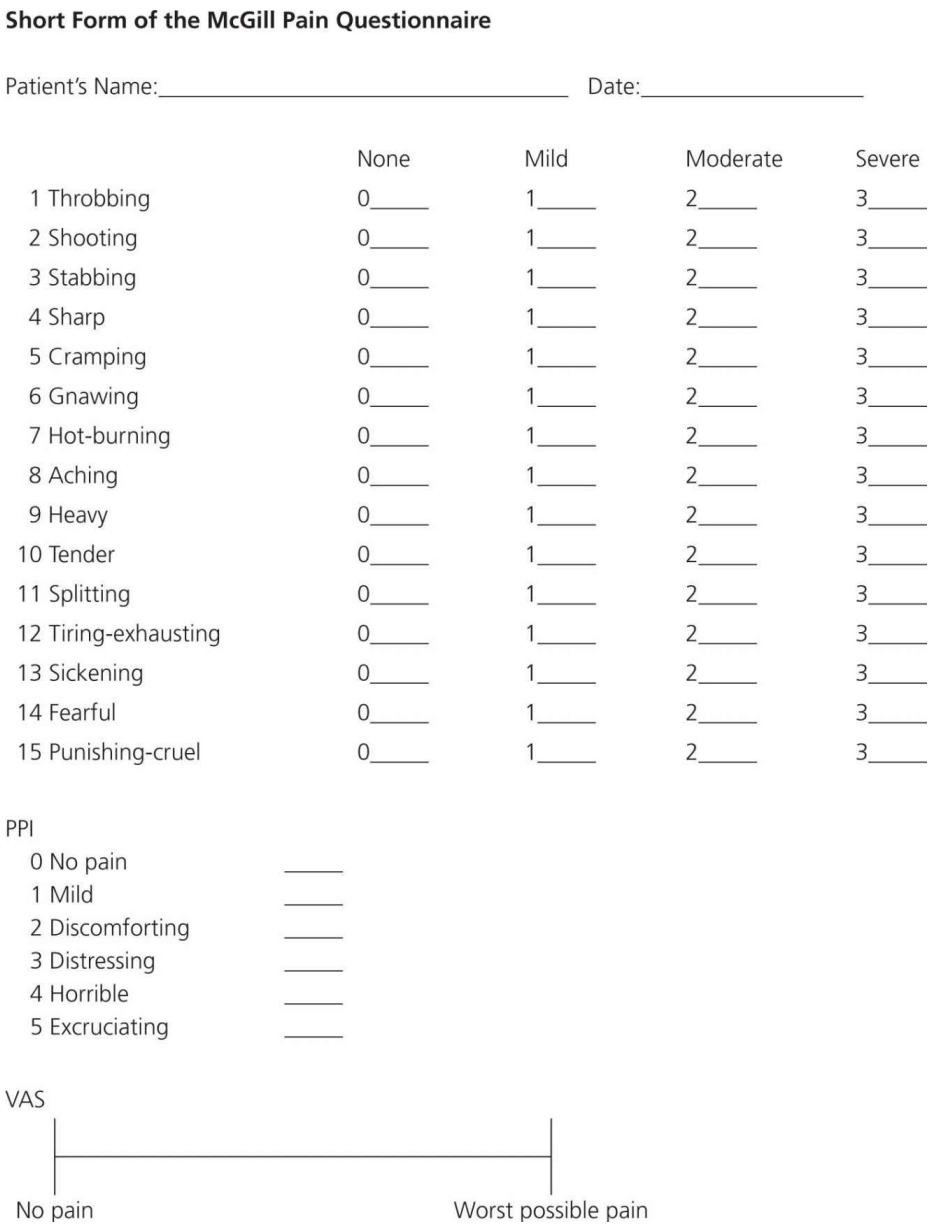
The MPQ has been shown to be a valid, objective, and reliable instrument [78]. It is one of the most widely used tests for pain assessment in both clinical and research settings and has been applied in diagnosis and research in a variety of pain problems. Its success has been further established by its translation or adaptation in many languages or cultures, including English, Dutch, French, German, Brazilian Portuguese, Norwegian, Swedish, Mexican American, and Turkish.

Although the full MPQ takes only 5 minutes to administer, a short form of the MPQ (SF-MPQ) was developed to be used in situations in which administration of the complete MPQ is too long (Fig. 6-6). The main component of the **SF-MPQ** consists of 15 descriptors (11 sensory and 4 affective) that are rated on an intensity scale from 0 to 3 (0 = none, 1 = mild, 2 = moderate, or 3 = severe). Three pain scores are derived from the sum of the intensity rank values of the words chosen for sensory, affective, and total descriptors. The SF-MPQ still includes the PPI index of the standard MPQ and a VAS for pain intensity [76].

Brief Pain Inventory

Pain, mainly during its chronic stage, is often associated with physical and functional disabilities. The Brief Pain Inventory (BPI) is useful to assess functional impact of pain on a person (Fig. 6-7). The first part of the BPI measures pain severity using four different VASs anchored by 0 representing “no pain” and 10 being “pain as bad as you can imagine.” The second part of the BPI measures how pain interferes with general activity, mood, walking, normal work,

relationships with others, sleep, and enjoyment of life. Similar to pain severity each functional item is ranked on an 11-point numeric scale, where 0 represents "does not interfere" and 10 denotes "completely interferes." The sum of the scores of the pain intensity items represents the pain intensity score and the sum of the scores on the pain interference items represents the interference score [27].



Short Form of the McGill Pain Questionnaire

Patient's Name:_____ Date:_____

	None	Mild	Moderate	Severe
1 Throbbing	0_____	1_____	2_____	3_____
2 Shooting	0_____	1_____	2_____	3_____
3 Stabbing	0_____	1_____	2_____	3_____
4 Sharp	0_____	1_____	2_____	3_____
5 Cramping	0_____	1_____	2_____	3_____
6 Gnawing	0_____	1_____	2_____	3_____
7 Hot-burning	0_____	1_____	2_____	3_____
8 Aching	0_____	1_____	2_____	3_____
9 Heavy	0_____	1_____	2_____	3_____
10 Tender	0_____	1_____	2_____	3_____
11 Splitting	0_____	1_____	2_____	3_____
12 Tiring-exhausting	0_____	1_____	2_____	3_____
13 Sickening	0_____	1_____	2_____	3_____
14 Fearful	0_____	1_____	2_____	3_____
15 Punishing-cruel	0_____	1_____	2_____	3_____

PPI

0 No pain _____
1 Mild _____
2 Discomforting _____
3 Distressing _____
4 Horrible _____
5 Excruciating _____

VAS

No pain — Worst possible pain

FIGURE 6-6 The short form of the McGill Pain Questionnaire (MPQ). The sum of the rank values is the rating. (Reprinted with permission from Melzack [76].)

painDETECT

The painDETECT questionnaire detects neuropathic pain components in adult patients with LBP [34] and is recommended for use by nonspecialists [35]. This questionnaire comprised seven questions that investigate the quality of neuropathic pain symptoms. It is not necessary to perform physical evaluation and it is self-administered by the patient (Fig. 6-8). The first five questions ask about the gradation of pain, scored from 0 to 5 (never = 0, hardly noticed = 1, slightly = 2, moderately = 3, strongly = 4, very strongly = 5). Question 6 asks about the pain course pattern, scored from –1 to 2, depending on which pain course pattern diagram is selected. Question 7 asks about radiating pain, answered as yes or no, and scored as 2 or 0, respectively. The total score can range from –1 to 38 and suggests the probability of an existing neuropathic pain element. A score of ≤12 suggests that pain is unlikely to have a neuropathic component (<15%), whereas a score of ≥19 indicates that pain is probable to have a neuropathic component (>90%). If 12 ≥ score ≤ 19, the result is inconclusive and a more detailed evaluation is needed [34].

STUDY ID #: DO NOT WRITE ABOVE THIS LINE HOSPITAL #:

Brief Pain Inventory (Short Form)

Date: _ _ / _ _ / _ _ _ Time: _ _ _ _ _ _

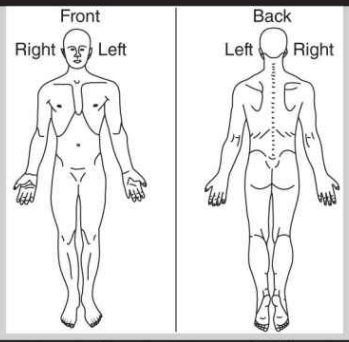
Name: _

Last First Middle initial

1. Throughout our lives, most of us have had pain from time to time (such as minor headaches, sprains, and toothaches). Have you had pain other than these everyday kinds of pain today?

1. Yes 2. No

2. On the diagram, shade in the areas where you feel pain. Put an X on the area that hurts the most.



3. Please rate your pain by circling the one number that best describes your pain at its worst in the last 24 hours.

0 1 2 3 4 5 6 7 8 9 10
No pain — Pain as bad as you can imagine

4. Please rate your pain by circling the one number that best describes your pain at its least in the last 24 hours.

0 1 2 3 4 5 6 7 8 9 10
No pain — Pain as bad as you can imagine

5. Please rate your pain by circling the one number that best describes your pain on the average.

0 1 2 3 4 5 6 7 8 9 10
No pain — Pain as bad as you can imagine

6. Please rate your pain by circling the one number that tells how much pain you have right now.

0 1 2 3 4 5 6 7 8 9 10
No pain — Pain as bad as you can imagine

STUDY ID #: DO NOT WRITE ABOVE THIS LINE HOSPITAL #:

Date: __/__/__ Time: ______

Name: ________________________

Last First Middle initial

7. What treatments or medications are you receiving for your pain?

8. In the last 24 hours, how much relief have pain treatments or medications provided? Please circle the one percentage that most shows how much **relief** you have received.

0%	10%	20%	30%	40%	50%	60%	70%	80%	90%	100%
No relief										Complete relief

9. Circle the one number that describes how, during the past 24 hours, pain has interfered with your:

	0	1	2	3	4	5	6	7	8	9	10
A. General activity	Does not interfere										Completely interferes
B. Mood	Does not interfere										Completely interferes
C. Walking ability	Does not interfere										Completely interferes
D. Normal work (includes both work outside the home and housework)	Does not interfere										Completely interferes
E. Relations with other people	Does not interfere										Completely interferes
F. Sleep	Does not interfere										Completely interferes
G. Enjoyment of life	Does not interfere										Completely interferes

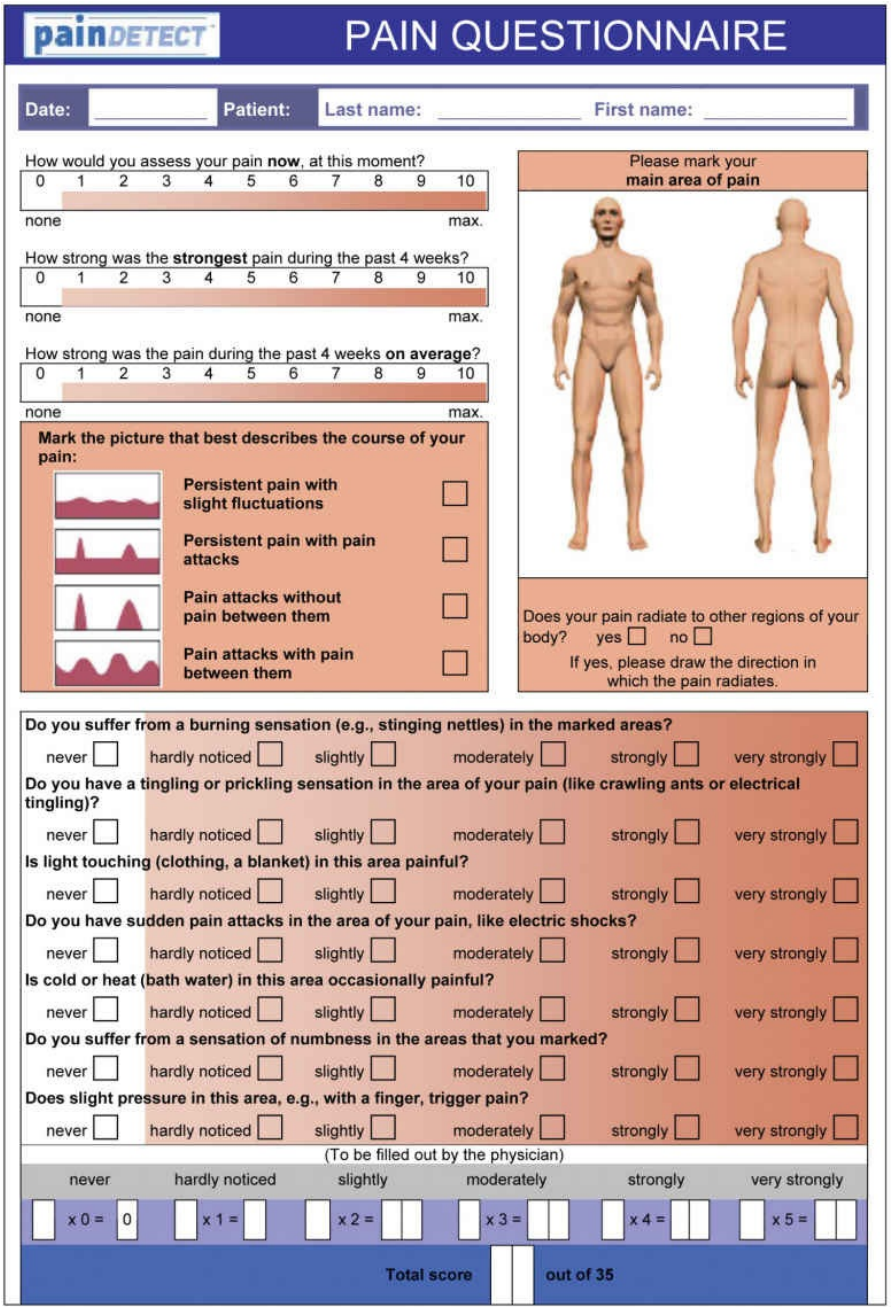
Page 2 of 2

FIGURE 6-7 Brief Pain Inventory (BPI) Form. (Reprinted with permission from Dr. Charles Cleeland, MD, Anderson Cancer Center.)

Psychological Questionnaires

It has become increasingly clear that a number of psychological factors can influence pain perception, and interfere with pain management strategies. Successful identification of potential confounding factors is critical to successful treatment and management of both acute and chronic pain patients, and to

prevent the transition from acute to chronic pain. These confounders include depression, anxiety, fear of pain and movement, and pain catastrophizing. People with depression, anxiety, high fear avoidance, high pain catastrophizing, or low-self-efficacy are at risk for development of chronic pain and for poor response to treatment in those with either acute or chronic pain (see Chapter 16). Although physical therapists are not trained in psychological interventions, they can screen for potential psychological factors that influence pain, incorporate psychological techniques into their plan of care, and refer to psychologists and family care for additional evaluation and management.


painDETECT

PAIN QUESTIONNAIRE

Date: Patient: Last name: First name:

How would you assess your pain **now**, at this moment?

0 1 2 3 4 5 6 7 8 9 10

none max.

How strong was the **strongest** pain during the past 4 weeks?

0 1 2 3 4 5 6 7 8 9 10

none max.

How strong was the pain during the past 4 weeks **on average**?

0 1 2 3 4 5 6 7 8 9 10

none max.

Mark the picture that best describes the course of your pain:

- **Persistent pain with slight fluctuations**
- **Persistent pain with pain attacks**
- **Pain attacks without pain between them**
- **Pain attacks with pain between them**

Please mark your **main area of pain**

Does your pain radiate to other regions of your body? yes no

If yes, please draw the direction in which the pain radiates.

Do you suffer from a burning sensation (e.g., stinging nettles) in the marked areas?

never hardly noticed slightly moderately strongly very strongly

Do you have a tingling or prickling sensation in the area of your pain (like crawling ants or electrical tingling)?

never hardly noticed slightly moderately strongly very strongly

Is light touching (clothing, a blanket) in this area painful?

never hardly noticed slightly moderately strongly very strongly

Do you have sudden pain attacks in the area of your pain, like electric shocks?

never hardly noticed slightly moderately strongly very strongly

Is cold or heat (bath water) in this area occasionally painful?

never hardly noticed slightly moderately strongly very strongly

Do you suffer from a sensation of numbness in the areas that you marked?

never hardly noticed slightly moderately strongly very strongly

Does slight pressure in this area, e.g., with a finger, trigger pain?

never hardly noticed slightly moderately strongly very strongly

(To be filled out by the physician)

never	hardly noticed	slightly	moderately	strongly	very strongly
x 0 = 0	x 1 =	x 2 =	x 3 =	x 4 =	x 5 =

Total score **out of 35**

FIGURE 6-8 The painDETECT is a questionnaire designed to evaluate the presence of neuropathic pain. (Modified from Freynhagen et al. [34] [Table 1].)

Fear-Avoidance Behaviors

The fear-avoidance model describes how individuals with chronic pain avoid activities on the basis of fear [110,112]. High fear-avoidance beliefs lead to reduced physical activity, reduced participation in rehabilitation, and poor outcomes in acute and chronic pain conditions. There are two commonly used

questionnaires to measure fear-avoidance beliefs:

The Fear-Avoidance Beliefs Questionnaire (FABQ) and the Tampa Scale of Kinesiophobia (TSK). *The FABQ* is a self-report questionnaire of 16 items. This tool focuses on patients' beliefs about how physical activity and work affect their current LBP. This questionnaire is based on fear theory and fear-avoidance cognitions including beliefs about the seriousness of the illness and its effect on the patient's life and on the concepts of somatic focusing and increased somatic awareness [112] (Fig. 6-9). Use of this questionnaire, as will be seen in Chapter 19, has been used in physical therapy practice to screen patients with acute LBP to place into specific treatment programs. The FABQ has been modified and validated for pain conditions in other body regions such as the shoulder and neck [38,62,81].

The *TSK* is a self-report 17-item survey that focuses on fear of movement and re-injury as a result of pain and has been used in a variety of chronic pain conditions including, back pain, fibromyalgia, neck pain, cancer pain, shoulder pain, and osteoarthritis [21,92,104]. This questionnaire is a 17-item questionnaire where patients rate their agreement with a series of statements on a 4-point Likert scale. Use of this questionnaire provides insights into the person's beliefs about their pain and can influence a plan of care. For example, if a person agrees with the statement "I'm afraid that I might injure myself if I exercise," then you may have difficulty with compliance in a home-exercise program.

Importantly, physical therapists' ratings of their perception of fear avoidance in patients with LBP do not correlate with either the FABQ or the TSK [22]. A 2-item screening questionnaire based on fear of physical activity and harm did correlate with the FABQ physical activity score. These two questions "Are you afraid of physical activity?" and "Are you afraid of harm?" may therefore be useful as a screen for further evaluation [22].

Pain Catastrophizing

Pain catastrophizing is a negative cognitive affective response to actual or potential pain. Pain catastrophizing has been conceptualized into three main categories: magnification, rumination, and a feeling of helplessness. Pain catastrophizing has proven an important construct with those who are high in pain catastrophizing reporting higher pain severity, greater disability, and greater illness behaviors. Further higher pain catastrophizing has been associated with negative pain-related adverse events such as higher chronic pain after injury and higher opioid usage [89]. The Pain Catastrophizing Scale, developed by Sullivan et al. [102], is a 13-item self-report questionnaire where items are rated on a 5-

point scale with 0 as not at all and 4 as all the time (Fig. 6-10). There is a total score and there are three subscales: magnification, rumination, and helplessness. The total score is computed by summing all responses to 13 items (0–52 range).

Fear-Avoidance Beliefs Questionnaire (FABQ)

Here are some of the things which other patients have told us about their pain. For each statement please circle a number from 0 to 6 to say how much physical activities such as bending, lifting, walking, or driving affect or would affect you back pain.

	Completely disagree			Unsure			Completely agree
1. My pain was caused by physical activity……	0	1	2	3	4	5	6
2. Physical activity makes my pain worse……..	0	1	2	3	4	5	6
3. Physical activity might harm my back……..	0	1	2	3	4	5	6
4. I should not do physical activities which (might) make my pain worse……..	0	1	2	3	4	5	6
5. I cannot do physical activities which (might) make my pain worse……	0	1	2	3	4	5	6

The following statements are about how your normal work affects or would affect your back pain.

	Completely disagree			Unsure			Completely agree
6. My pain was caused by my work or by an accident at work……..	0	1	2	3	4	5	6
7. My work aggravated my pain……..	0	1	2	3	4	5	6
8. I have a claim for compensation for my pain……..	0	1	2	3	4	5	6
9. My work is too heavy for me……..	0	1	2	3	4	5	6
10. My work makes or would make my pain worse……	0	1	2	3	4	5	6
11. My work might harm my back……..	0	1	2	3	4	5	6
12. I should do my normal work with my present pain……..	0	1	2	3	4	5	6
13. I cannot do my normal work with my present pain……..	0	1	2	3	4	5	6
14. I cannot do my normal work till my pain is treated……..	0	1	2	3	4	5	6
15. I do not think that I will be back to my normal work within 3 months ……	0	1	2	3	4	5	6
16. I do not think that I will ever be able to go back to that work……	0	1	2	3	4	5	6

Scoring:

Scale 1: fear-avoidance beliefs about work—Items 6, 7, 9, 10, 11, 12, 15.

Scale 2: fear-avoidance beliefs about physical activity—Items 2, 3, 4, 5.

FIGURE 6-9 Fear-Avoidance Belief Questionnaire. (Reprinted with permission from Waddell et al. [112].)

Self-Efficacy Questionnaires

There are numerous self-efficacy questionnaires available to understand the functional impact of pain on a person. In general these questionnaires expand upon the BPI and use VAS or NRS to assess the impact of pain on activities of daily living and social function. The use of a self-efficacy questionnaire is invaluable in understanding the pain experience. We have included two published and validated questionnaires that are used for people with chronic pain conditions as examples and are given in Figs. 6-11 and 6-12. The Pain Self-efficacy Questionnaire is self-efficacy scale used for people in chronic pain that also asks the respondents to take pain into account when rating their self-efficacy beliefs (see items in Fig. 6-11). All items include mention of performing the activities despite their pain (e.g., "I can do most of the household chores (e.g., tidying-up, washing dishes), despite the pain") [82].

We are interested in the types of thoughts and feelings that you have when you are in pain. Listed below are thirteen statements describing different thought or feelings that may be associated with pain. Using the following scale, please indicate the degree to which you have these thoughts and feelings when you are experiencing pain.

	0 Not at all	1 To a slight degree	2 To a moderate degree	3 To a great degree	4 All the time
1. I worry all the time about whether the pain will end.	0	1	2	3	4
2. I feel I can't go on.	0	1	2	3	4
3. It's terrible and I think it's never going to get any better.	0	1	2	3	4
4. It's awful and I feel that it overwhelms me.	0	1	2	3	4
5. I feel I can't stand it anymore.	0	1	2	3	4
6. I become afraid that the pain may get worse.	0	1	2	3	4
7. I think of other painful experiences.	0	1	2	3	4
8. I anxiously want the pain to go away.	0	1	2	3	4
9. I can't seem to keep it out of my mind.	0	1	2	3	4
10. I keep thinking about how much it hurts.	0	1	2	3	4
11. I keep thinking about how badly I want the pain to stop.	0	1	2	3	4
12. There is nothing I can do to reduce the intensity of the pain.	0	1	2	3	4
13. I wonder whether something serious will happen.	0	1	2	3	4

FIGURE 6-10 Pain Catastrophizing Scale. (Modified from Sullivan [102].)

The Chronic Pain Self-Efficacy Scale (CPSS) (Fig. 6-12) is designed to measure chronic pain patients' perceived self-efficacy to cope with its consequences. Each item in the CPSS is presented as a question by the examiner to the patient (e.g., "How certain are you that you can decrease your pain quite a bit?") [4]. The patient is then asked to respond on a 10-point Likert scale from

10 “very uncertain” to 100 “very certain.” Fig. 6-12 lists the questions for the CPSS. As can be seen in Fig. 6-12 there are three different domains for self-efficacy: (1) pain management, (2) physical function, and (3) coping.

Psychological Screening Questions

STarT Back Screening Tool

STarT Back Screening Tool (SBST) is a brief screening questionnaire designed for directing initial treatment for LBP in primary care. It classifies the risk of poor prognosis in individuals with LBP with or without radiculopathy influenced by physical and psychosocial factors [49], and can predict future dysfunction in patients with LBP in the primary care setting [8]. When SBST was used to stratify and assign to a treatment plan, patients showed greater functionality on the Rolland-Morris Disability Questionnaire, better quality of life, less use of health care services, and less absenteeism compared with the patients who were not stratified [50].

Self-efficacy for pain management (PSE)

1. How certain are you that you can decrease your pain quite a bit?
2. How certain are you that you can continue most of your daily activities?
3. How certain are you that you can keep your pain from interfering with your sleep?
4. How certain are you that you can make a small-to-moderate reduction in your pain by using methods other than taking extra medication?
5. How certain are you that you can make a large reduction in your pain by using methods other than taking extra medications?

Self-efficacy for physical function (PFE)

1. How certain are you that you can walk ½ mile on flat ground?
2. How certain are you that you can lift a 10-pound box?
3. How certain are you that you can perform a daily home exercise program?
4. How certain are you that you can perform your household chores?
5. How certain are you that you can shop for groceries or clothes?
6. How certain are you that you can engage in social activities?
7. How certain are you that you can engage in hobbies or recreational activities?
8. How certain are you that you can engage in family activities?
9. How certain are you that you can perform the work duties you had prior to the onset of chronic pain? (For homemakers, please consider your household activities as your work duties.)

Self-efficacy for coping with symptoms (CSE)

1. How certain are you that you can control your fatigue?
2. How certain are you that you can regulate your activity so as to be active without aggravating your physical symptoms (e.g., fatigue, pain)?
3. How certain are you that you can do something to help yourself feel better if you are feeling blue?
4. As compared to other people with chronic medical problems like yours, how certain are you that you can manage your pain during your daily activities?
5. How certain are you that you can manage your physical symptoms so that you can do the things you enjoy doing?
6. How certain are you that you can deal with the frustration of chronic medical problems?
7. How certain are you that you can cope with mild to moderate pain?
8. How certain are you that you can cope with severe pain?

FIGURE 6-11 Pain Self-Efficacy Questionnaire. (Reprinted with permission from Nicholas [82] [Appendix A].)

The SBST questionnaire consists of nine items. Four of them are related to referred leg pain, disability, and comorbid shoulder or neck pain. The other five statements correspond to a psychosocial subscale (items 5–9), which analyses bothersomeness, pain catastrophizing, fear, anxiety, and depression. Patients are asked to either agree or disagree with each of the nine items, except for bothersomeness, as it uses a Likert scale (ranging from not at all to extremely bothersome). Both total score (Q 1–9) and psychosocial subscale score (Q 5–9) are calculated. Scores <4 allocate the patient to the low-risk group. However, scores of ≥4 on the psychosocial subscale allocate a patient to the high-risk group. A score ≥4 but <4 on the psychosocial subscale allocates a patient to the medium-risk group. The SBST takes approximately 2 minutes to complete and is available at http://www.keele.ac.uk/sbst/. Generic 5-question and 9-question screening questionnaires for those without LBP are also available at the website.

Please note 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. *(Total Score (sum of 1-10)* _____*)*
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 enjoy things, despite the pain

0	1	2	3	4	5	6
Not at all confident						Completely confident

2. I can do most of the household chores (e.g., tidying up, washing dishes, etc.), despite the pain.

0	1	2	3	4	5	6
Not at all confident						Completely confident

3. I can socialize with my friends and family members as often as I used to do, despite the pain.

0	1	2	3	4	5	6
Not at all confident						Completely confident

4. I can cope with my pain in most situations.

0	1	2	3	4	5	6
Not at all confident						Completely confident

5. I can do some form of work, despite the pain (work indicates housework, paid and unpaid work).

0	1	2	3	4	5	6
Not at all confident						Completely confident

6. I can still do many of the things I enjoy doing, such as hobbies and leisure activity, despite the pain.

0	1	2	3	4	5	6
Not at all confident						Completely confident

7. I can cope with my pain without medication.

0	1	2	3	4	5	6
Not at all confident						Completely confident

8. I can still accomplish most of my goals in life, despite the pain.

0	1	2	3	4	5	6
Not at all confident						Completely confident

9. I can still live a normal lifestyle, despite the pain.

0	1	2	3	4	5	6
Not at all confident						Completely confident

10. I can gradually become more active, despite the pain.

0	1	2	3	4	5	6
Not at all confident						Completely confident

FIGURE 6-12 Chronic Pain Self-Efficacy Scale items. Questionnaires are delivered to the subject and the subject rates their response on a 10-point Likert scale from very uncertain to very certain. (Reprinted with permission from Anderson et al. [4] [Appendix A].)

Screening for Anxiety and Depression

Although physical therapists are neither trained nor qualified to diagnose anxiety and depression, there are simple screening questions available that can be easily

incorporated into a history and physical. If a subject is positive on these screening questions, referral back to the doctor, primary care physician, and/or a psychologist would be appropriate. Depression screening questions based on the Patient-Health Questionnaire (PHQ-2) has been validated and is based on the first two items of the PHQ-9 [98]. Alternatively, Haggman et al. [44] validated a 2-question depression screening. For anxiety, the Generalized Anxiety Disorder (GAD-7) similarly has a 2-question screening GAD-2 that has been validated and recommended for use in primary care [59]. The PHQ and the GAD questionnaires can be found on the American Psychological Association website (http://www.apa.org/pi/about/publications/caregivers/practice-settings/assessment/tools/patient-health.aspx).

- Depression screening questions (PHQ-2): Over the last 2 weeks how often have you been bothered by any of the following problems: (1) little interest or pleasure in doing things and (2) feeling down, depressed, or hopeless. Subjects are asked to answer not at all, several days, more than half the days, or nearly every day [98].
- Depression screening questions: (1) “During the past month, have you often been bothered by feeling down, depressed or hopeless?” (2) “During the past month, have you often been bothered by little interest or pleasure in doing things?” [44].
- Anxiety screening questions (GAD-2): Over the last 2 weeks how often have you been bothered by the following problems: (1) feeling nervous, anxious, or on edge? (2) not being able to stop or control worrying? Subjects are asked to answer not at all, several days, more than half the days, or nearly every day [59].

Quality of Life

Pain is a central factor affecting quality of life for who have diseases characterized by chronic pain. A treatment’s effectiveness should not only be assessed for its impact on pain but also for its impact on quality of life. An understanding of the impact of pain on quality of life will guide development of a plan of care for the subject. *The SF-36 Health Survey Questionnaire* contains 36 items, which takes about 5 minutes to complete. It measures health on eight multi-item dimensions, covering functional status (Physical functioning, Social functioning, Role limitations [physical problems], Role limitations), well-being (Mental health, Vitality, Pain), and overall evaluation of health (General health perception, Health change). The SF-36 questionnaire is able to detect positive as

well as negative states of health. In six of the eight dimensions patients are asked to rate their responses on 3- or 6-point scales (box) rather than simply responding yes or no (Fig. 6-13). For each dimension, item scores are coded, summed, and transformed on to a scale from 0 (worst health) to 100 (best health) [18].

Another tool proposed by the World Health Organization (WHO) is the *WHO Quality of Life Assessment* (WHOQOL). This is a generic quality-of-life instrument that was designed to be applicable to people living under different circumstances, conditions, and cultures [114,115]. Two versions are available: the full WHOQOL, WHOQOL-100 (100 items), and the short version, WHOQOL-BREF (26 items). The WHOQOL-100 produces scores relating to particular facets of quality of life (e.g., positive feelings, social support, financial resources), scores relating to larger domains (e.g., physical, psychological, social relationships) and a score relating to overall quality of life and general health. The WHOQOL-BREF produces domain scores, but not individual facet scores (Fig. 6-14). Regarding somatic diseases, the WHOQOL-100 has good to excellent validity and reliability [97]. It is based on a Likert-type scale and is scored from 1 to 5, with higher scores indicating a better quality of life.

Disease-Specific Questionnaires

There are a number of disease-specific questionnaires that are designed to assess issues directly related to the particular disease and have proven useful when evaluating particular diseases. These questionnaires include the Fibromyalgia Impact Questionnaire [19], the Oswestry Disability Questionnaire [32], the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) [7], and the Disabilities of the Arm, Shoulder and Hand [6]. These questionnaires are commonly utilized in clinical trial research and have increasingly been utilized in clinical practice. In a diverse clinical practice, however, it is difficult to utilize a variety of disease-specific questionnaires and therefore they are typically utilized in specialty clinics. However, if one runs a chronic back pain clinic the use of the Oswestry Disability Questionnaire may prove more useful than self-efficacy questionnaires listed above.

SF-36 QUESTIONNAIRE

(1992 - Medical Outcomes Trust)

This survey asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities.

Please answer these questions by "check-marking" your choice. Please select only one choice for each item.

1. In general, would you say your health is:

1. Excellent 2. Very good 3. Good 4. Fair 5. Poor

2. Compared to ONE YEAR AGO, how would you rate your health in general NOW?

1. MUCH BETTER than one year ago.
2. Somewhat BETTER now than one year ago.
3. About the SAME as one year ago.
4. Somewhat WORSE now than one year ago.
5. MUCH WORSE now than one year ago.

3. The following items are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

Activities	**1. Yes, limited a lot**	**2. Yes, limited a little**	**3. No, not limited at all**
a) Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports?	1. Yes, limited a lot	2. Yes, limited a little	3. No, not limited at all
b) Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf?	1. Yes, limited a lot	2. Yes, limited a little	3. No, not limited at all
c) Lifting or carrying groceries?	1. Yes, limited a lot	2. Yes, limited a little	3. No, not limited at all
d) Climbing several flights of stairs?	1. Yes, limited a lot	2. Yes, limited a little	3. No, not limited at all

e) Climbing one flight of stairs?	1. Yes, limited a lot	2. Yes, limited a little	3. No, not limited at all
f) Bending, kneeing or stooping?	1. Yes, limited a lot	2. Yes, limited a little	3. No, not limited at all
g) Walking more than a mile?	1. Yes, limited a lot	2. Yes, limited a little	3. No, not limited at all
h) Walking several blocks?	1. Yes, limited a lot	2. Yes, limited a little	3. No, not limited at all
i) Walking one block?	1. Yes, limited a lot	2. Yes, limited a little	3. No, not limited at all
j) Bathing or dressing yourself?	1. Yes, limited a lot	2. Yes, limited a little	3. No, not limited at all

4. During the past 4 weeks, have you had any of the following problems with your work or other regular activities as a result of your physical health?

	Yes	**No**
a) Cut down on the amount of time you spent on work or other activities?	1. Yes	2. No
b) Accomplished less than you would like?	1. Yes	2. No
c) Were limited in the kind of work or other activities?	1. Yes	2. No
d) Had difficulty performing the work or other activities (for example it took extra effort)?	1. Yes	2. No

5. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

	Yes	**No**
a) Cut down on the amount of time you spent on work or other activities?	1. Yes	2. No
b) Accomplished less than you would like?	1. Yes	2. No
c) Didn't do work or other activities as carefully as usual?	1. Yes	2. No

6. During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?
1. Not at all 2. Slightly 3. Moderately 4. Quite a bit 5. Extremely

7. How much bodily pain have you had during the past 4 weeks?
1. None 2. Very mild 3. Mild 4. Moderate 5. Severe 6. Very severe

8. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?
1. Not at all 2. A little bit 3. Moderately 4. Quite a bit 5. Extremely

9. These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the past 4 week …

	1. All of the time	**2. Most of the time**	**3. A good bit of the time**	**4. Some of the time**	**5. A little of the time**	**6. None of the time**
a) Did you feel full of pep?	1. All of the time	2. Most of the time	3. A good bit of the time	4. Some of the time	5. A little of the time	6. None of the time
b) Have you been a very nervous person?	1. All of the time	2. Most of the time	3. A good bit of the time	4. Some of the time	5. A little of the time	6. None of the time

c) Have you felt so down in the dumps that nothing could cheer you up?	1. All of the time	2. Most of the time	3. A good bit of the time	4. Some of the time	5. A little of the time	6. None of the time
d) Have you felt calm and peaceful?	1. All of the time	2. Most of the time	3. A good bit of the time	4. Some of the time	5. A little of the time	6. None of the time
e) Did you have a lot of energy?	1. All of the time	2. Most of the time	3. A good bit of the time	4. Some of the time	5. A little of the time	6. None of the time
f) Have you felt downhearted and blue?	1. All of the time	2. Most of the time	3. A good bit of the time	4. Some of the time	5. A little of the time	6. None of the time
g) Do you feel worn out?	1. All of the time	2. Most of the time	3. A good bit of the time	4. Some of the time	5. A little of the time	6. None of the time
h) Have you been a happy person?	1. All of the time	2. Most of the time	3. A good bit of the time	4. Some of the time	5. A little of the time	6. None of the time
i) Did you feel tired?	1. All of the time	2. Most of the time	3. A good bit of the time	4. Some of the time	5. A little of the time	6. None of the time

10. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc.)?
1. All of the time
2. Most of the time.
3. Some of the time
4. A little of the time.
5. None of the time.

11. How TRUE or FALSE is each of the following statements for you?

	1. Definitely true	**2. Mostly true**	**3. Don't know**	**4. Mostly false**	**5. Definitely false**
a) I seem to get sick a little easier than other people?	1. Definitely true	2. Mostly true	3. Don't know	4. Mostly false	5. Definitely false
b) I am as healthy as anybody I know?	1. Definitely true	2. Mostly true	3. Don't know	4. Mostly false	5. Definitely false
c) I expect my health to get worse?	1. Definitely true	2. Mostly true	3. Don't know	4. Mostly false	5. Definitely false
d) My health is excellent?	1. Definitely true	2. Mostly true	3. Don't know	4. Mostly false	5. Definitely false

FIGURE 6-13 Short Form-36 Quality of Life Questionnaire. (Reprinted with permission from Medical Outcomes Trust and Quality Metric Inc.)

Physical and Functional Examination for Pain

In addition to the assessment of pain through pain scales and questionnaires, using objective measures of hyperalgesia or function is useful. Patient's ability to engage in functional activities can be assessed by numerous self-report tools. Those measures can assess the severity of pain during activities such as to walking up and down stairs, sitting for a specific time, lifting specific weights, or performing activities of daily living. There is a good correspondence among self-reports, disease characteristics, physical therapists' or physicians' ratings of functional abilities, and objective functional performance [31,54].

The following questions ask how you feel about your quality of life, health, or other areas of your life. I will read out each question to you, along with the response options. **Please choose the answer that appears most appropriate.** If you are unsure about which response to give to a question, the first response you think of is often the best one.

		Very poor	Poor	Neither poor nor good	Good	Very good
1.	How would you rate your quality of life?	1	2	3	4	5
		Very dissatisfied	**Dissatisfied**	**Neither satisfied nor dissatisfied**	**Satisfied**	**Very satisfied**
2.	How satisfied are you with your health?	1	2	3	4	5

The following questions ask about **how much** you have experienced certain things in the last four weeks.

		Not at all	A little	A moderate amount	Very much	An extreme amount
3.	To what extent do you feel that physical pain prevents you from doing what you need to do?	5	4	3	2	1
4.	How much do you need any medical treatment to function in your daily life?	5	4	3	2	1
5.	How much do you enjoy life?	1	2	3	4	5
6.	To what extent do you feel your life to be meaningful?	1	2	3	4	5
		Not at all	**A little**	**A moderate amount**	**Very much**	**Extremely**
7.	How well are you able to concentrate?	1	2	3	4	5
8.	How safe do you feel in your daily life?	1	2	3	4	5
9.	How healthy is your physical environment?	1	2	3	4	5

The following questions ask about how completely you experience or were able to do certain things in the last four weeks.

		Not at all	A little	Moderately	Mostly	Completely
10.	Do you have enough energy for everyday life?	1	2	3	4	5
11.	Are you able to accept your bodily appearance?	1	2	3	4	5
12.	Have you enough money to meet your needs?	1	2	3	4	5

13.	How available to you is the information that you need in your day-to-day life?	1	2	3	4	5
14.	To what extent do you have the opportunity for leisure activities?	1	2	3	4	5

		Very poor	**Poor**	**Neither poor nor good**	**Good**	**Very good**
15.	How well are you able to get around?	1	2	3	4	5
		Very dissatisfied	**Dissatisfied**	**Neither satisfied nor dissatisfied**	**Satisfied**	**Very satisfied**
16.	How satisfied are you with your sleep?	1	2	3	4	5
17.	How satisfied are you with your ability to perform your daily living activities?	1	2	3	4	5
18.	How satisfied are you with your capacity for work?	1	2	3	4	5
19.	How satisfied are you with yourself?	1	2	3	4	5
20.	How satisfied are you with your personal relationships?	1	2	3	4	5
21.	How satisfied are you with your sex life?	1	2	3	4	5
22.	How satisfied are you with the support you get from your friends?	1	2	3	4	5
23.	How satisfied are you with the conditions of your living place?	1	2	3	4	5
24.	How satisfied are you with your access to health services?	1	2	3	4	5
25.	How satisfied are you with your transport?	1	2	3	4	5

The following question refers to how often you have felt or experienced certain things in the last four weeks.

		Never	**Seldom**	**Quite often**	**Very often**	**Always**
26.	How often do you have negative feelings such as blue mood, despair, anxiety, depression?	5	4	3	2	1

[The following table should be completed after the interview is finished]

		Equations for computing domain scores	Raw score	Transformed scores*	
				4–20	0–100
27.	Domain 1	(6-Q3) + (6-Q4) + Q10 + Q15 + Q16 + Q17 + Q18 ( ) + ( ) + ( ) + ( ) + ( ) + ( ) + ( )	a. =	b:	c:
28.	Domain 2	Q5 + Q6 + Q7 + Q11 + Q19 + (6-Q26) ( ) + ( ) + ( ) + ( ) + ( ) + ( )	a. =	b:	c:
29.	Domain 3	Q20 + Q21 + Q22 ( ) + ( ) + ( )	a. =	b:	c:
30	Domain 4	Q8 + Q9 + Q12 + Q13 + Q14 + Q23 + Q24 + Q25 ( ) + ( ) + ( ) + ( ) + ( ) + ( ) + ( ) + ( )	a. =	b:	c:

FIGURE 6-14 The World Health Organization Quality of Life Survey (WHOQOL). (Reprinted with permission from the World Health Organization.)

Commonly used functional assessment scales are the Roland-Morris Disability Scale [67], the Functional Status Index [54], and the Oswestry Disability Scale [32]. A more extensive instrument, the Sickness Impact Profile, includes over 150 questions to examine a range of physical activities and psychological features [9].

Range of Motion

Physical therapists routinely assess range of motion (ROM) of specific joints. Assessing active and passive ROM can give valuable information on limitations. To further understand the nature of the pain, Maitland [67] suggests examining the point in the ROM when pain first becomes painful (P1) and the point in the ROM when a person must stop because of pain (P2). This type of assessment can prove extremely valuable in understanding the nature and irritability of the pain so that a treatment plan can be individualized to the subject. For example, compare two patients with the same diagnosis, lateral epicondylalgia, that both have full passive ROM. In Patient 1, his P1 for elbow flexion is 10 degrees and P2 is 30 degrees. In Patient 2, his P1 for elbow flexion is 60 degrees and P2 is full ROM. Patient 1 is clearly limited in his abilities because of the pain and is highly irritable. Patient 2 has full active ROM despite pain increasing at 60 degrees and is therefore not as irritable as Patient 1. Thus, a treatment approach for patient 1 should be geared toward pain reduction and exercise should proceed more slowly. On the other hand, Patient 2 can be treated more aggressively with active exercise and manual therapies as needed.

Strength

Assessment of strength and the impact of pain on strength is a highly useful skill. Several conditions generally arise where pain and strength are interrelated. First, strength can be limited as a result of pain. Full muscle contraction may not be possible because of pain. In this case, reducing pain will have an immediate effect on strength. On the other hand, a decrease in strength of a particular muscle may result in abnormal function of the joint, and thus result in pain. In this case, one must strengthen the weakened muscle to reduce pain and thus relief of pain may be delayed. Third, as a result of long-standing disuse there may be a loss of strength in a particular muscle or muscle groups. In this case, strengthening of the muscle or muscle groups is necessary to return the patient to full functional status. However, there may be little impact of strengthening directly on the pain.

Hyperalgesia and Allodynia

Measurement of hyperalgesia to mechanical stimuli can be done with a pressure algometer (Fig. 6-15A) by examining the pressure pain threshold both at the site of injury (i.e., primary hyperalgesia) and outside the site of injury (i.e., secondary hyperalgesia). These measures will give the therapist an understanding of the underlying mechanisms of the pain condition the patient is presenting with. Primary hyperalgesia will assess pain resulting from peripheral factors. However, if secondary hyperalgesia exists, then a patient is likely to have alterations in the central processing of nociceptive stimuli.

A

B

FIGURE 6-15 A: Measurement of hyperalgesia with a pressure algometer. B: Measurement of allodynia with a von Frey filament.

Allodynia, a painful response to nonpainful stimuli, particularly of the extremities (hand and feet), is commonly measured using von Frey filaments (Semmes Weinstein monofilaments) (Fig. 6-15B). This is an extremely useful measure in people with neuropathic pain or complex regional pain syndrome, or postoperatively [5]. Using graded forces applied to the skin, a threshold for pain response can be assessed. Under normal conditions, only high forces will

produce pain. However, after nerve injury, complex regional pain syndrome, or operation, the threshold decreases to a level that is considered allodynia. One can also assess allodynia by brushing the skin with a cotton whisp or with sophisticated graded stimuli [66]. People with allodynia would clearly have a strong central component to their pain.

Functional Measures

There are several functional tests that are commonly utilized to assess the impact of pain on speed and function. In general these are timed tests and have been found valuable for people with both acute and chronic pain. For measures of endurance the 6-minute walk test measures the distance a person can walk in 6 minutes. For strength, the sit-to-stand test records the time taken to come from sitting to standing five times. For speed and endurance, the timed up and go test is commonly utilized. In this test the subject is asked to stand from sitting and walk a distance of 100 ft, return, and sit back down. The time at which a person performs this task is then recorded. Numbers of 10 seconds and less are considered within normal range [14]. For balance, the loaded reach task uses a standard weight, such as 5% body weight, and holds the weight initially as shoulder height close to the body and then reaches forward as far as possible. The distance the person can reach is then recorded. Other tests include the 50 ft walk test (the time taken by a person to walk 50 ft; speed measure, normal 8–9 seconds) and repeated trunk flexion (time taken to flex and extend the trunk five times; normal 14–16 seconds) [84]. Normative values over the life span are available for comparison for all of these tests. These tests described here are particularly useful for people with lower extremity pain, such as osteoarthritis, lower back pain, or people with chronic widespread pain, such as fibromyalgia. Similar measures for people with upper extremity pain or cervical pain could be used to assess function. These measures are particularly useful to document progress and to document effectiveness of treatment. Novy et al. [84] analyzed several measures within lower back pain patients and determined that these functional factors fall into one of two categories: speed and coordination or endurance and strength.

PAIN ASSESSMENT IN SPECIAL POPULATIONS

Most of the assessment measures described above have been used in cognitively

intact adults, but some also apply to other populations. This section outlines special considerations in pain assessment for newborns, children, and adolescents, and neurologically or cognitively impaired individuals.

Newborn

Assessment of the pain experience in infant and young children populations is regularly limited by their inability to verbalize pain or localize the source of their pain [52]. The infant, unless paralyzed or comatose, provides the health care practitioner with signals of pain through a variety of physiologic and behavioral communication such as oral expression/cries; facial expression; rigid body posture; clenched hands or toes; body movements, such as withdrawal from a painful stimulus, limpness, or flaccidity in preterm or ill infants; altered sleep patterns; and inconsolability [33,99]. As can be seen, the use of these signals to rate pain is both indirect and inferential [52]. Parents play a crucial role when evaluating their infant's pain. Most parents can distinguish pain behaviors in their baby quite easily and this should be included in pain assessment [24,60,80].

Many tools have been developed to assess infant's pain in several acute pain conditions. The Neonatal Facial Coding System (NFCS) is a systematic description of infant pain expression [43] (Fig. 6-16). This coding system provides a detailed, anatomically based, and objective description of the infant's reactions to potentially painful events. The NFCS is used to score for the presence or absence (scored 0 or 1) of 10 discrete facial actions, namely brow bulge, eye squeeze, naso-labial furrow, open lips, vertical mouth stretch, horizontal mouth stretch, lip purse, taut tongue, tongue protrusion, and chin quiver. The NFCS has been validated and recently been used to study pain responses in children up to 18 months of age [65].

Another instrument that has been widely used for evaluating infant's pain is Neonatal Infant Pain Scale (NIPS), which quantifies the level of pain on a scale from 0 to 7 on the basis of five behavioral characteristics: facial expressions, crying, movements of arms and legs, and the state of arousal. In addition, breathing pattern is used as a physiological parameter [61]. NIPS is very easy and quick to use (Fig. 6-17).

Children

A number of tools or scales for assessing children's pain have been developed in the last three decades. They can be classified as physiologic,

behavioral/observational, or self-report, depending on the nature of the response that is measured [64]. Many factors can modify pain perception in children, including age, gender, cognitive level, previous experience with pain, family learning, and culture. These factors are usually stable in contrast to many cognitive, behavioral, and emotional factors, which vary depending on the situation, and can greatly modify a child's perception and expression of pain [68,69].

Action	Description
Brow bulge	Bulging, creasing and vertical furrows above and between brows occurring as a result of the lowering and drawing together of the eyebrows.
Eye squeeze	Identified by the squeezing or bulging of the eyelids. Bulging of the fatty pads about the infant's eyes is pronounced.
Naso-labial furrow	Primarily manifested by the pulling upwards and deepening of the naso-labial furrow (a line or wrinkle which begins adjacent to the nostril wings and runs down and outwards beyond the lip corners.
Open lips	Any separation of the lips I scored as open lips.
Stretch mouth (vertical)	Characterized by a tautness at the lip corners coupled with a pronounced downward pull on the jaw. Often stretch mouth is seen when an already wide open mouth is opened a fraction further by an extra pull at the jaw.
Stretch mouth (horizontal)	This appears as a distinct horizontal pull at the corners of the mouth.
Lip purse	The lips appear as if an 'oo' sound is being pronounced.
Taut tongue	Characterized by a raised, cupped tongue with sharp tensed edges. The first occurrence of taut tongue is usually easy to see, often occurring with a wide open mouth. After this first occurrence, the mouth may close slightly. Taut tongue is still scorable on the basis of the still visible tongue edges.
Chin quiver	An obvious high frequency up-down motion of the jaw.

FIGURE 6-16 Neonatal Facial Coding System (NFCS). If the action does not occur, point = 0. If the action occurs, point = 1. NFCS score greater than 3 indicates pain. (Reprinted with permission from Grunau and Craig [43].)

Pain assessment		Score
Facial expression		
0- Relaxed Muscles	Restful face, neutral expression	
1- Grimace	Tight facial muscles; furrowed brow, chin, jaw (negative facial expression – nose, mouth and brow)	
Cry		
0- No Cry	Quiet, no crying	
1- Whimper	Mild moaning, intermittent	
2- Vigorous Cry	Loud scream; rising, shrill, continuous (Note: silent cry may be scored if baby is intubated by evidenced of obvious mouth and facial movement)	
Breathing patterns		
0- Relaxed	Usual pattern for this infant	
1- Change in Breathing	Indrawing, irregular, faster than usual; gagging, breath holding	
Arms		
0- Relaxed/ Restrained	No muscular rigidity; occasional random movement of arms	
1- Flexed/ Extended	Tense, straight legs; rigid and/or rapid extension, flexion	
Legs		
0- Relaxed/ Restrained	No muscular rigidity; occasional random movement of arms	
1- Flexed/ Extended	Tense, straight legs; rigid and/or rapid extension, flexion	
State of arousal		
0- Sleeping/ Awake	Quiet, peaceful sleeping or alert random leg movement	
1- Fussy	Alert, restless, and trashing	

FIGURE 6-17 Neonatal/Infant Pain Scale (NIPS). Recommended for children less than 1 year old. A score greater than 3 indicates pain. (Reprinted with permission from Children's Hospital of Eastern Ontario.)

Most 2-year-old children can report the presence and location of pain, but they do not have the cognitive skills needed yet to describe pain intensity until about 3 or 4 years of age. Generally, most 3-year-old children can use a three-level pain intensity scale with simple terms such as "no pain," "a little pain," or "a lot of pain." Four-year-old children can usually manage 4- or 5-item scales [26,40,48,53].

Probably the most commonly used assessment tool for children is The Faces Pain Scale. This scale consists of seven gender-neutral faces depicting "no pain" (neutral face) to "most pain possible" expressions, placed at equal intervals horizontally [12]. The children are instructed to point to the face that shows how much pain they feel. Ordered faces are scored from 0 to 6. Variations of this scale are shown in Fig. 6-18A and B and include the Wong–Baker FACES Pain Scale (Fig. 6-18A) [116] and The Faces Pain Scale-Revised (Fig. 6-18B). These scales have been validated for use in both acute and chronic disease-related pain.

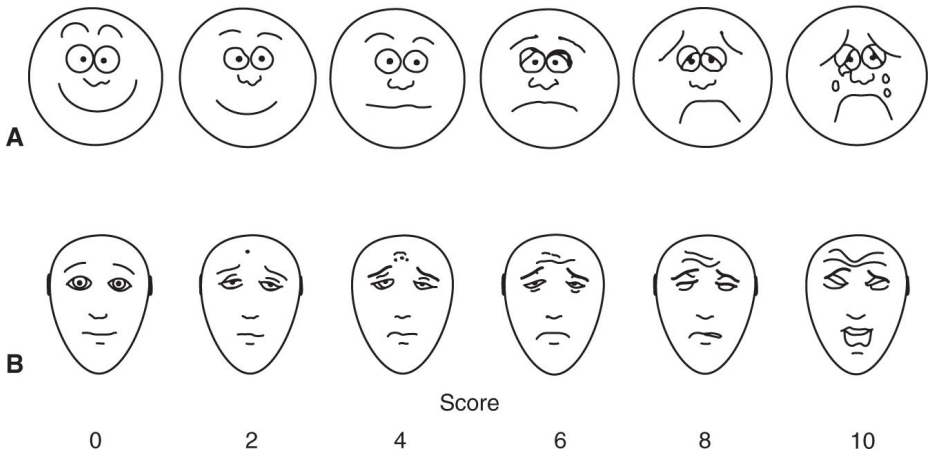


FIGURE 6-18 A: Wong-Baker Faces Pain Scale. (Reprinted with permission from Wong and Baker [116] [Figure 3].) B: Face Pain Scale–Revised. (Reprinted with permission from Bieri et al. [12].)

When children are approximately 8 years of age, they are able to rate the quality of pain [71,93]. Thus, school-aged children and adolescents can also use verbal NRSs, originally studied in adults to assess pain intensity (see more details in section "Pain Assessment in Adults" above).

Quantitative scales such as the VAS [26], the Colored Analog Scale (CAS) [72], and numerical scales require more complex concepts and skills that generally emerge between 5 and 7 years. The CAS is similar to a VAS and was developed specifically for assessing pain in children. The CAS varies in three dimensions—color, width, and length—so that children can more easily understand that different scale positions reflect different values in pain intensity. Recent investigation has shown equivalent psychometric properties to a VAS [107]. This tool appears to be simple and easy to administer, making it practical for clinical use.

On the other hand, adolescents indicate preference for VAS and NRS [41]. The Adolescent Pediatric Pain Tool [93,94] and the Pediatric Pain Questionnaire [109] are examples of multidimensional pain measures used with older children and adolescents. The MPQ [75,76] is an example of an adult pain measure that has been used in clinical practice with older adolescents (see details in section "Pain Assessment in Adults" above). In summary, there are many excellent pediatric self-report measures, and their clinical application requires careful consideration of age, developmental, and measurement issues [85].

Patients with Neurological or Cognitive Impairment

Unfortunately, some patients with dementia or neurological disorders (memory,

language, cognition) and critically ill or nonverbal children with serious cognitive disability are not able to offer an accurate evaluation about their own pain. Damage to the central nervous system affects memory, language, and higher-order cognitive processing necessary to communicate the experience. Yet, despite changes in central nervous system functioning, persons with dementia still experience pain sensation to a degree similar to that of the cognitively intact older adult [95]. Although self-report of pain is often possible in those with mild to moderate cognitive impairment, as dementia progresses, the ability to self-report decreases and eventually self-report is no longer possible. Patients with severe dementia or neurological disorders are generally unable to provide self-report of pain verbally, in writing, or by other means [79,86]. Critiques of existing nonverbal pain assessment tools indicate that, although there are tools with potential, there is no tool that has strong reliability and validity that can be recommended for broad adoption in clinical practice for persons with advanced dementia [46,101,118].

Facial expressions, verbalizations/vocalizations, body movements, changes in interpersonal interactions, changes in activity patterns or routines, and mental status changes have been identified as categories of potential pain indicators in older persons with dementia. Some behaviors are common and typically considered pain related (e.g., facial grimacing, moaning, groaning, rubbing a body part), but others are less obvious (e.g., agitation, restlessness, irritability, confusion, combativeness, particularly with care activities or treatments, or changes in appetite or usual activities) and require follow-up evaluation such as response to known analgesics. Tools for evaluating pain in patients with dementia are in varying stages of the development and validation process. Those with the strongest conceptual and psychometric support at this time, as well as clinical utility, are cited in Herr et al.'s article [45] for which we refer the reader for additional information if needed in their practice setting. Furthermore, guidelines and position statements have been released that focus on pain assessment in the older adult and individuals unable to self-report [1,45,47].

CONCLUSION

In summary, a battery of tests and measures should be utilized to assess both acute and chronic pain. Although generally acute pain is considered a symptom, it can have a huge impact on function and quality of life. Depression and anxiety interfere with response to treatment and should be recognized and addressed

accordingly. Chronic pain clearly has a multidimensional nature and impacts function and quality of life. Understanding the multidimensional nature of pain, the impact of pain on function and the impact of pain on quality of life are vital to effective treatment. Further fear of pain and avoidance of activity as well as pain catastrophizing are common in both acute and chronic pain conditions. Treatment of an individual who is afraid of re-injury will likely involve a multidisciplinary approach using the biopsychosocial model. This is important for both acute and chronic pain conditions. However, for some people fear of pain is not a problem, and the classic overachiever may constantly reinjure themselves. In this case use of the biopsychosocial model may be inappropriate and the use of the biomedical model for treatments may be more important. A more comprehensive multidimensional pain assessment that includes location and meaning of pain enhances clinicians' knowledge about a child's or an adolescent's pain experience and helps to prevent clinician's misunderstandings about that pain.

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CHAPTER 7

General Principles of Physical Therapy Practice

Kathleen A. Sluka

PRINCIPLES OF PHYSICAL THERAPY PRACTICE

The practice of physical therapy involves providing service to people that have impairments, functional limitations, disabilities, or changes in physical function and health status resulting from injury or disease [1]. Physical therapists interact and collaborate with other health professions to provide health care to restore, maintain, and promote optimal physical function (Fig. 7-1). Related to pain, physical therapists are primarily involved in preventing the progression of impairments, functional limitations, and disabilities that may result from either the acute condition that produces pain, or from the chronic pain condition itself. Specifically for chronic pain, restoration and promotion of optimal physical function to promote an improved quality of life is a critical role for physical therapists. For chronic pain, it is important to recognize that although the ultimate goal is a reduction in pain, pain relief may be minimal or not occur. However, physical function and quality of life may be greatly improved.

The evaluation process determines the impairments, functional limitations, disabilities, or changes in physical function. In pain management, restoration of function involves the use of education and exercise, as well as a variety of manual therapies, and electrophysical agents. In acute pain management, the goals of therapy are aimed at reducing pain, decreasing peripheral inflammatory processes, and maintaining function. For chronic pain management the goals of therapy are similarly aimed at reducing pain and improving function. Likely multiple treatment procedures will be involved in this process. The physical therapist should make an educated treatment choice on the basis of known mechanisms of action and clinical effectiveness.

The *Guide to Physical Therapy Practice*, updated in 2014, was developed by the American Physical Therapy Association to assist practicing physical therapists in their choice of tests and measures, and treatments. The guide recommends that coordination of care, education, therapeutic exercise, and functional training form the core of physical therapy plans of care. In addition, other interventions should be added to a treatment plan as necessary to address findings in the evaluation procedure. For pain management, these other interventions include manual therapy, electrotherapy, and heat and cold therapy. A plan of care is generally developed that takes into account the individual in terms of personal and environmental factors as well as the current health or biology underlying the disease or disorder. In general, the patient will need to have an active treatment plan to gain full independent functional status and control their pain (Fig. 7-2). The addition of nonpharmacological interventions to the plan of care gives the patient a nondrug choice for managing their pain. The plan may come in stages and will certainly be individualized and based on patient preferences. There may be times within an individual's treatment plan when the pain is severe enough that it needs to be managed by passive treatments, like transcutaneous electrical nerve stimulation (TENS) or pharmaceutical agents, and subjects will not participate in an active program. There may be other times when fear of movement or pain catastrophizing is high and these will need to be addressed for someone to fully participate in the active program.

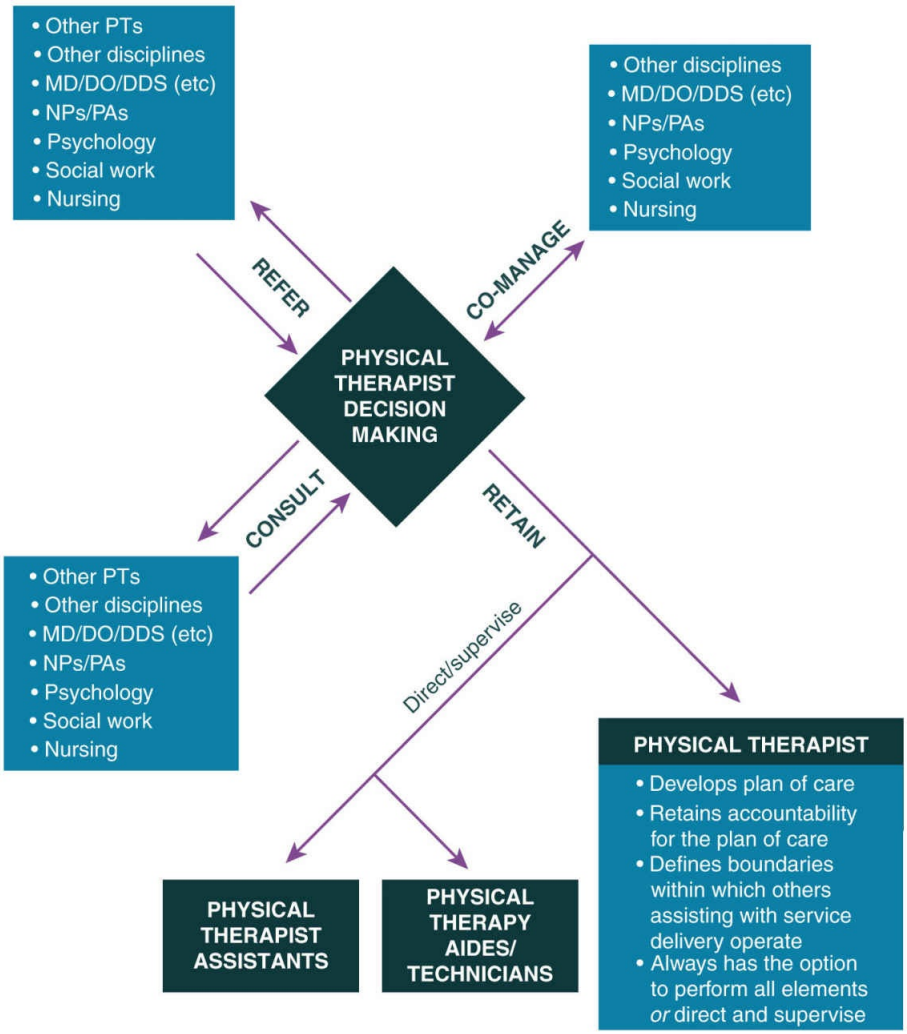

FIGURE 7-1 General guidelines for physical therapy treatment from the "Guide to Physical Therapy Practice" [1].

Further, treatment of pain, either acute or chronic, involves a multidisciplinary approach that includes medical management, physical therapy, and psychological management. The goals for pain management, especially for chronic pain conditions, include the patient as an active participant. Specifically, physical therapy treatments should emphasize activity and the emphasis should be on improved function rather than on the impairment. All treatment plans should be based on evidence, both basic science and clinical.

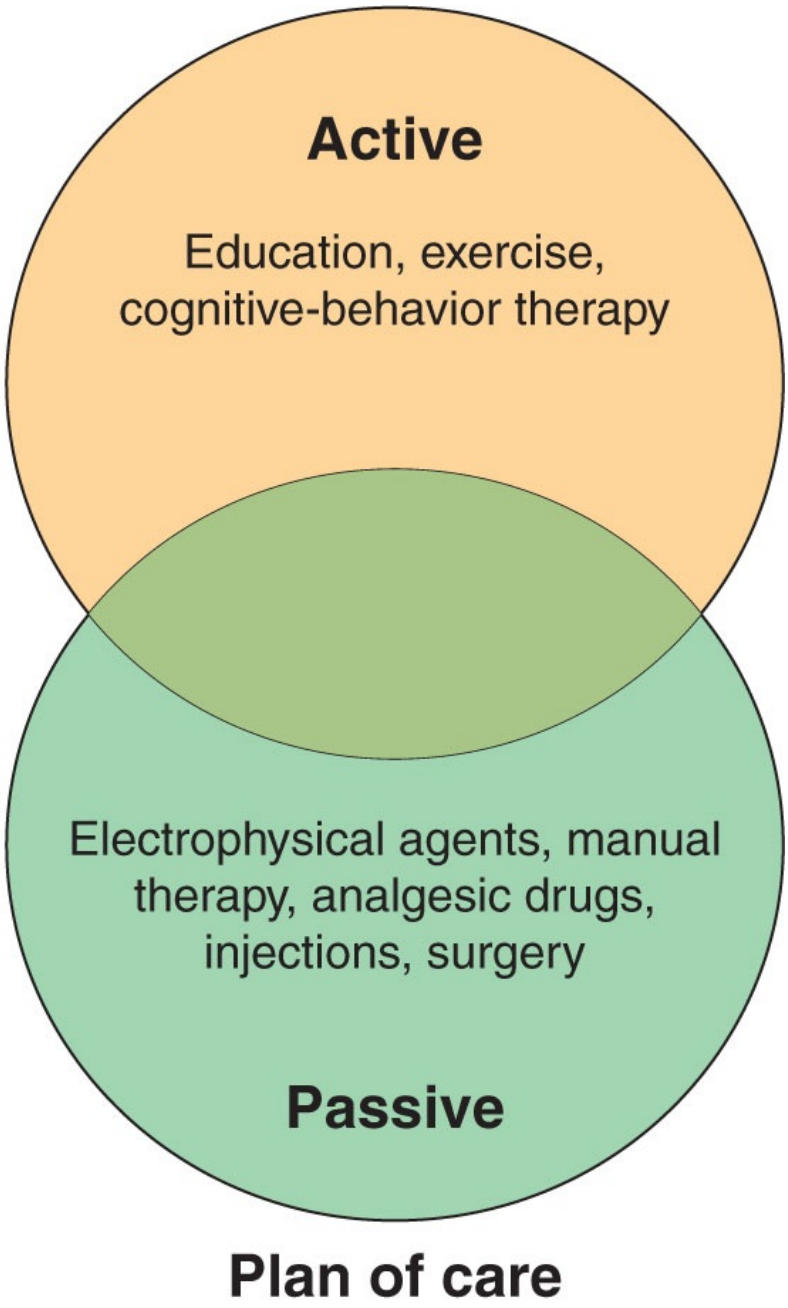

FIGURE 7-2 Outline of a plan of care that illustrated active and passive physical therapy treatment choices for pain.

OVERVIEW OF MECHANISM-BASED APPROACH TO PAIN MANAGEMENT

Using a mechanism-based approach to pain management has been proposed by

investigators to individualize the plan of care [12,14]. The current anatomical based classification system (i.e., low back pain, shoulder pain) is limiting. The underlying neural mechanisms may be tissue based (i.e., nerve, muscle, joint) and thus are not uniquely different between the knee joint and the shoulder joint. To be clear, there are different biomechanical approaches for the knee and shoulder, but the neural transmission of nociceptive stimuli will be similar if it comes from injury to the muscles surrounding the shoulder or the muscles surrounding the knee. Thus, anatomical sites are less important than the tissue affected for transmission of pain.

A mechanism-based approach would also involve understanding of basic mechanisms underlying pain, as well as potential psychological confounders that could interfere with improved outcomes. Recent studies suggest that there is substantial variability in the healthy controls and in people with pain in terms of their pain-processing physiology and in their psychological states [7,9,13] (see Chapter 5). For example, although people with fibromyalgia as a group show a loss of conditioned pain modulation compared with healthy controls, there are some people with fibromyalgia that have normal conditioned pain modulation and some healthy controls that have a loss of conditioned pain modulation (Fig. 7-3). Understanding this variability is essential in designing an appropriate plan of care. Despite this individual variability between subjects, population-based data can give a general idea of what signs and symptoms are most common and therefore what to test. It is increasingly clear that significant portions of individuals with chronic pain show (1) reduced central inhibition and enhanced central excitability, (2) neuropathic pain signs symptoms, and (3) changes in peripheral tissues and nociceptors. Thus, the mechanism-based approach is multifactorial and involves tissue specificity, basic neural mechanisms, and psychosocial modifiers.

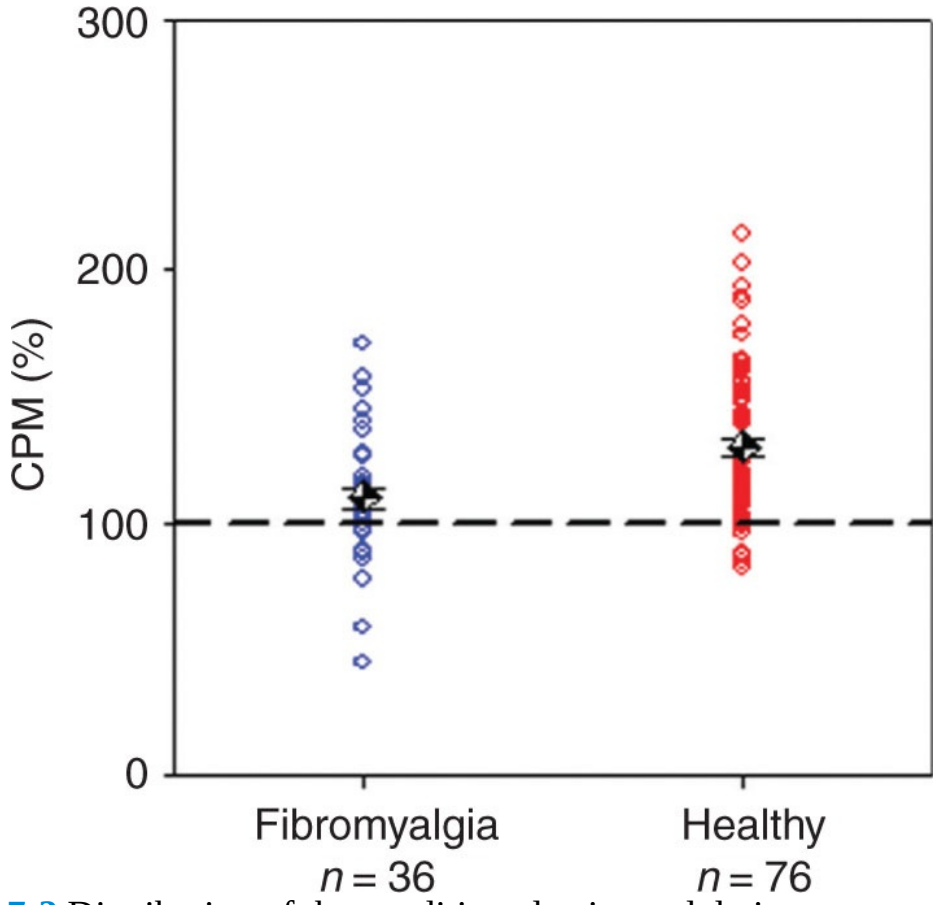

FIGURE 7-3 Distribution of the conditioned pain modulation response in people with fibromyalgia compared with healthy control subjects without pain. The white and black diamond represents the mean for each group with the SEM. Data are compiled from raw data from multiple experiments to illustrate the differences between conditions. CPM, central pain modulation pathway.

A schematic representation of three categories to consider when designing a plan of care for individuals with acute or chronic pain is illustrated in Fig. 7-4 and has been previously outlined by Phillips and Clauw [12]. These mechanistic-based categories include **nociceptive pain,** which is defined as pain as a result of activation of nociceptors. This is common in individuals with an injury, inflammation, or mechanical irritant, for example, those with an ankle sprain or rheumatoid arthritis would fall into this category. It is easily determined for those with acute injury and is generally associated with localized pain to the site of injury. Nociceptive pain and activation of nociceptors can also result in enhanced central excitability and people can present with referred pain and secondary hyperalgesia. In this case, the nociceptor activation is generally driving these central manifestations. **Neuropathic pain** arises because of lesion or disease of the somatosensory system. This could occur because of direct injury to the nerve

or nerve branches, or from metabolic diseases such as diabetes (see Chapter 21 for more detail). Common examples encountered by physical therapists include diabetic neuropathy, carpal tunnel syndrome, and complex regional pain syndrome. Patients can be assessed with the painDETECT and will present with negative signs such as loss of sensation or motor function, as well as positive signs such as dysesthesia. **Central pain** conditions are due to a disturbance in central pain processing that show as enhanced central excitability and loss of central inhibition. Classic examples are fibromyalgia, temporomandibular disorder, and nonspecific low back pain. This is more difficult to determine in a patient but can be associated with a loss of conditioned pain modulation, enhanced temporal summation to repetitive noxious stimuli as well as more diffuse symptoms such as widespread and referred pain, fatigue, sleep disturbances, and/or cognitive dysfunction.

A schematic diagram (Fig. 7-5) shows how underlying peripheral and central sensitization can lead to pain. In people with primarily peripheral sensitization, the enhanced nociceptor activity activates unsensitized central neurons to result in pain. Conversely, in people where there is no peripheral sensitization, after an injury has healed for example, a normal input from a nociceptor will activate a sensitized central neuron to result in pain. Lastly, in many conditions, there will be both enhanced peripheral and central neuron activity (i.e., sensitization) that will lead to pain. Removal of only the peripheral input in some cases will reduce a nociceptor-driven central sensitization. In other cases, removal of the peripheral input will have a partial effect and residual central sensitization can remain so that the patient continues to feel pain.

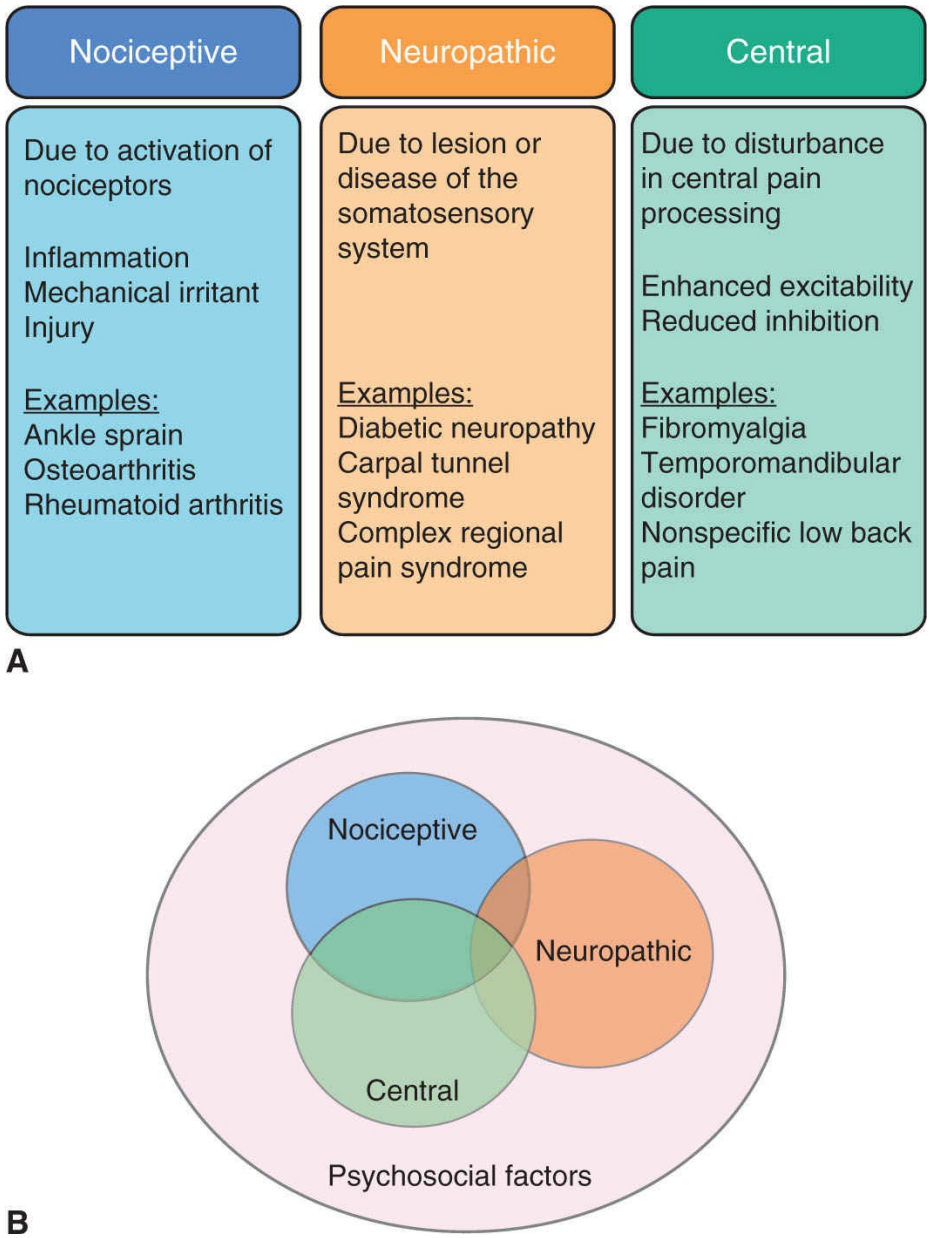

FIGURE 7-4 Schematic diagrams representing a mechanistic approach to pain management. A: Mechanisms included are nociceptive, neuropathic, or central. People with pain can have can just one type of pain, or, more commonly observed, can have a combination of different mechanisms underlying their pain. B: Illustrates the overlap between different mechanisms of pain (nociceptive, neuropathic, and central) and further illustrates that psychosocial factors can influence any of these components to modulate pain.

It has become increasingly clear that psychosocial factors can influence the perception of pain and recovery of pain (see Chapter 16). Negative factors such as pain catastrophizing, anxiety, or fear can all enhance any of the three

mechanisms of pain (Fig. 7-4), and can maintain a painful condition longer than normal healing time. These psychological factors are hypothesized to be critical in the transition from acute to chronic pain and have been shown to be predictive of the development of chronic pain postoperatively. Therefore, successful therapy must evaluate and incorporate therapies to address a variety of these psychosocial factors. As previously stated, treating maladaptive psychosocial factors is not only important in treating a person with chronic pain but is important for maximizing effectiveness of therapy in the acute condition and potentially preventing the development of chronic pain.

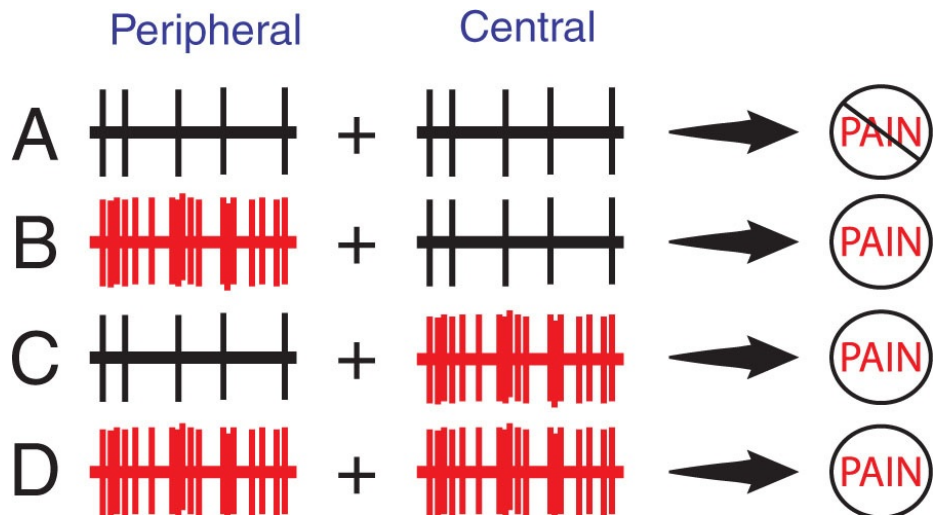

FIGURE 7-5 A schematic diagram shows how underlying peripheral and central sensitization can lead to pain. A: Shows the condition with no pain. Normal nociceptor and central neuron activity in most cases may not produce pain. B: Shows a condition with primarily peripheral sensitization. Enhanced nociceptor activity activates unsensitized central neurons to result in pain. C: Illustrates a condition where there is central sensitization without peripheral sensitization. Normal input from a nociceptor will activate a sensitized central neuron to result in pain. D: Illustrates a condition where there is both peripheral and central sensitization resulting in pain. Removal of only the peripheral input in some cases will reduce a nociceptor-driven central sensitization. In other cases removal of the peripheral input will have a partial effect and residual central sensitization can remain so that the patient continues to feel pain.

MECHANISMS OF ACTION OF PHYSICAL THERAPY INTERVENTIONS

Several theories have been proposed to explain the mechanisms of pain relief for physical therapy interventions. These include activation of gate control mechanisms, counterirritant, activation of endogenous opioids, and restoration of function to remove a peripheral irritant. The gate control theory generally states that activation of large-diameter afferents will reduce nociceptive activity in the dorsal horn of the spinal cord. Thus, any modality that activates large-diameter afferents could be explained by the gate control theory of pain. However, in some cases, we have more data on pharmacological mechanisms that expand upon the gate control theory and provide additional data for a more effective treatment. The counterirritant theory suggests that applying a painful stimulus will activate endogenous pain control mechanisms that reduce pain. For a modality to be a counterirritant it would therefore need to be painful. Thus, hot packs and electrotherapy are likely not counterirritants. However, an ice bath may indeed be a counterirritant and could produce pain through this "mechanism." Indeed there is a large body of evidence that uses noxious cold stimuli to activate central pain modulation pathways (CPMs). CPM is induced by application of a noxious stimulus in one, outside of the pain threshold testing site, and results in an increase in pain threshold in areas distant from the noxious stimuli. Activation of endogenous opioid pathways, through the PAG-RVM pathway, mediates the effects of electrotherapy and aerobic exercise, and thus these pathways can be activated by nonpainful physical therapy interventions. Activation of this pathway would result in decreased dorsal horn neuron activity, and decreased nociceptive input to higher brain centers, and thus reduction in pain. Lastly, through exercise or manual therapies, one can increase range of motion and return normal function to a joint or tissue to eliminate a mechanical irritant. Removal of the irritant would reduce activation of a nociceptor and thus reduce input to the central nervous system and consequently the brain for perception of pain.

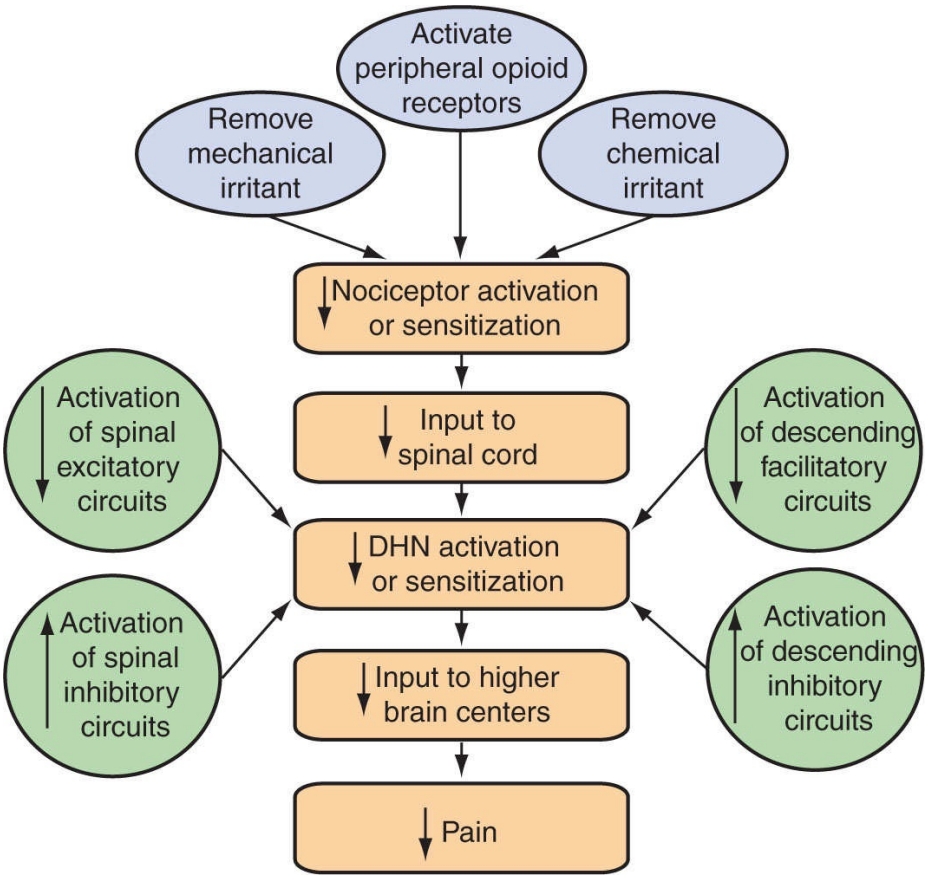

FIGURE 7-6 Schematic diagram to explain potential basic science mechanisms for the actions of physical therapy treatments to reduce pain. In general, treatments will have effects peripherally that will reduce nociceptor input and sensitization, or centrally that will decrease dorsal horn neuron activity and sensitization. DHN = dorsal horn neuron.

Fig. 7-6 outlines the potential mechanisms by which physical therapy interventions can reduce pain. Interventions are generally aimed at treating the periphery and reducing peripheral sensitization of primary afferent fibers, or the central nervous system and reducing central sensitization. In the periphery, removal of the peripheral mechanical or chemical irritant causing sensitization of nociceptors would reduce input to the spinal cord, thus reducing dorsal horn neuron sensitization. Alternatively, one could activate peripheral opioid receptors located on sensitized nociceptors, which would reduce nociceptive input to the spinal dorsal horn decreasing sensitization of dorsal horn neurons. Reducing activation of dorsal horn neurons reduces input to higher brain centers and thus reduces pain. Heat, cold, and manual therapy have all been shown to have peripheral effects that remove mechanical or chemical irritants, whereas low-frequency TENS and aerobic exercise activate peripheral opioid receptors.

Centrally, therapies are aimed at decreasing activation of spinal excitatory circuits or decreasing facilitation from supraspinal sites. Alternatively, physical therapy interventions can increase local spinal inhibitory circuits or descending supraspinal inhibition. Together this will reduce sensitization of dorsal horn neurons, decreasing input to higher brain centers and decrease pain. TENS, manual therapy, and exercise generally work to either reduce central excitation and/or increase central inhibition.

Guidelines for an effective plan of care need to be based on an adequate evaluation. The evaluation should be geared toward determining the peripheral and central components to the pain condition, if neuropathic components exist, and if there are confounding psychological components (see Chapter 16). Interventions can then be aimed at addressing these different pathways, peripheral, neuropathic, central conditions, and any overlying psychological confounders. In recent years, there has been substantial research into the mechanisms by which physical therapy interventions reduce pain. These basic mechanisms will be elaborated on in the following chapters as they relate to a specific therapy.

PLACEBO AND NOCEBO EFFECTS

All interventions for pain have a placebo effect and have sometimes been considered a nonspecific effect (see Chapter 8 for more details). The placebo effect for pain is defined as a reduction in pain by the intervention's symbolic effect, rather than as a result of a specific therapeutic effect. The placebo is easily manipulated and can influence the effectiveness of treatment, and should be utilized to assess efficacy of treatment for pain. The placebo effect for pain relief, interestingly, is reversed by the opioid receptor antagonist, naloxone [10], suggesting activation of descending opioid inhibitory pathway. Neuroimaging studies confirm activation of regions involved in opioid analgesia including the prefrontal cortex, the anterior cingulate cortex, and the periaqueductal gray and medulla (see references [6,11]). Thus, the placebo effect is real, activates endogenous opioid pathways, and should be utilized to enhance efficacy of treatment.

The control of supraspinal pathways over nociceptive activity can not only produce an enhanced analgesic effect (i.e., placebo), but can also produce a decreased effectiveness or enhanced pain (i.e., nocebo). As with the placebo, there are known biological mechanisms underlying the nocebo. Blockade of

cholecystokinin (CCK) receptors with proglumide prevents the nocebo effect on pain relief [2,3,8]. CCK is involved in opioid tolerance producing an antiopioid effect when released [8]. Imaging studies show that the nocebo activates similar pathways to that of the placebo: anterior cingulate, prefrontal, and insular cortices [8]. Thus, the nocebo is also real and utilizes antiopioid mechanisms to enhance pain. As a clinician, one should also be careful not to produce a nocebo effect. Interactions with patients should, therefore, always be positive and encouraging to enhance therapeutic efficacy of any given treatment, and to avoid a negative interaction with the intervention.

As an example, George et al. [4] investigated the effects of patient expectation on effectiveness of spinal manipulation. In this study they gave instructions that suggested the intervention was very effective, ineffective, or had unknown effects. Increases in pain thresholds occurred in the group that was instructed with a positive expectation, decreases in pain threshold occurred in the group that was instructed with a negative expectation, and no change occurred in the group that received the neutral expectation. Thus, delivery of a treatment technique by the therapist is critical to obtain full effectiveness.

AN EVIDENCE-BASED APPROACH FOR PHYSICAL THERAPY

There are several types of evidence that can be utilized to make an educated decision on the treatment of choice. This evidence includes basic science mechanisms, effects in experimental pain models, randomized placebo-controlled trials, and systematic reviews or meta-analysis (Fig. 7-7). All types of evidence can be utilized to obtain an educated evidence-based plan of care. Many treatments will use multiple types of evidence to support their plan of care making the choice of therapy stronger.

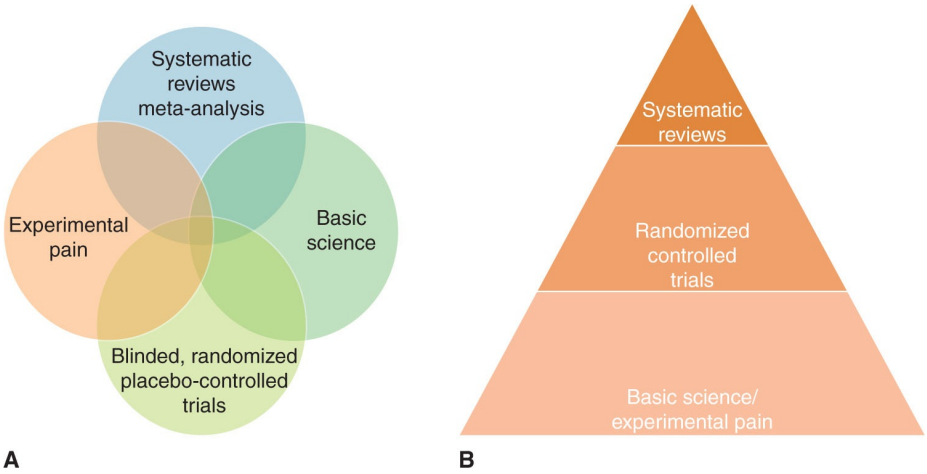

FIGURE 7-7 Schematic diagrams for the types of evidence that can be used to the use of physical therapy treatments. The hierarchical scheme includes basic science and experimental pain studies in human subjects as the base, randomized controlled trials, and systematic reviews and meta-analysis of the clinical literature.

Health care professionals, including physical therapists, need to develop reliable plan of care choices on the basis of the evidence. There is a wealth of available information that is difficult for the healthcare professional to read and synthesize. Reviews can be unscientific and biased in the way they collect data and summarize the information. Therefore, systematic reviews and meta-analysis attempt to minimize these biases and provide a reliable basis for clinical decision making. A hierarchy of evidence is often utilized and is outlined in Fig. 7-7B. At the top of the level of evidence is systematic reviews and meta-analysis. Systematic reviews and meta-analysis utilize multiple randomized controlled trials in an attempt to allow health professionals to make evidence-based clinical decisions. If available, systematic reviews and meta-analysis would therefore provide the top level of evidence to support a particular intervention. However, caution should be utilized for negative results given that these systematic reviews are based on the quality of the randomized controlled trials used to make such decisions. In particular, appropriate dosing is often not taken into consideration for physical therapy interventions in the randomized controlled trials, and subsequently not taken into consideration in the systematic reviews, making the evidence negative or inconclusive (see Chapter 11 for examples). The gold standard for clinical evidence is a randomized, double-blind, placebo-controlled trial. True double-blinding of the therapist and patient for many of physical therapy interventions is difficult to achieve. Placebos, for some therapies, such as hot packs or exercise, are difficult to achieve. Many physical therapy interventions are compared against another therapy or medication to

provide a means of assessing efficacy without a placebo treatment. Further, in many randomized controlled trials, the person examining the effects of treatment is blinded to the treatment allocation, and thus, provides blinding to a treatment in the absence of a true placebo. At the bottom of the hierarchy are typically basic science mechanisms or effects in experimental pain conditions. Subsequent chapters will describe the levels of evidence in terms of the basic science mechanisms, randomized controlled trials, and where available systematic reviews from the Cochrane Library or meta-analysis. For recommendations of evidence-based practice, systematic reviews from the Cochrane Library will be used as the primary source, and followed with systematic reviews and meta-analysis from the primary literature. If systematic reviews or meta-analysis of interventions are unavailable, randomized controlled trials will be described to support treatment recommendations.

Ethical questions that routinely arise in the application of therapy are related to therapeutic efficacy of the intervention. Should clinicians deliver and bill for an intervention that does not produce an analgesic effect above a placebo response? Should clinicians deliver and bill for interventions that do not have clinical evidence to support their effectiveness? What is the minimal level of evidence required for a clinician to deliver and bill for treatment? Is it acceptable to utilize strong basic science evidence alone or in conjunction with nonrandomized controlled trials to support the choice of treatment? Obviously in a perfect world, where evidence is abundant and gives a clear positive or negative response for an intervention, the answer is clear. If systematic reviews of high-quality evidence show a negative effect of the intervention, then one should probably not choose that intervention, unless as a last resort. If systematic reviews of the evidence, on the other hand, show a positive effect of the intervention for a given pain condition, one should use that intervention in the plan of care. For example, there is strong evidence for the effectiveness of aerobic conditioning exercise in people with fibromyalgia from systematic reviews [5]. Therefore, any plan of care for a person with fibromyalgia should include an aerobic conditioning program.

SUMMARY

The practice of physical therapy is typically aimed at finding and eliminating the physical cause of the pain using a variety of techniques including exercises as well as manual therapies and modalities. For acute pain conditions associated

with tissue damage and nociceptive pain this biomedical approach to pain management may be adequate and likely to be successful. However, one should be cognizant of the fact that even in acute pain conditions and surgery, psychosocial factors can interfere with recovery, and facilitate the transition from acute to chronic pain. Thus, someone with an anterior cruciate ligament tear that goes for surgery who has high levels of anxiety, or significant fear avoidance behaviors, might not participate in rehabilitation, and could be at risk for poor outcome and development of chronic pain. Further, once pain becomes chronic this model of practice needs modification and should always include an interdisciplinary approach in the plan of care. At this stage physical therapy practice should shift to enhance the active involvement of the patient with education on activity modification and exercise while minimizing passive interventions such as manual therapy and electrophysical agents. Manual therapy and electrophysical agents should ideally be utilized in people with chronic pain as an adjunct to the active exercise-oriented approach. The plan of care may vary depending on the state of the individual at any given time and could include primarily active interventions, primarily passive interventions, or a combination of both. Furthermore, in some patients with the acute pain, the pain is not proportional to the amount of tissue damage and thus likely involves significant amounts of central nervous system changes and psychosocial variables that need to be addressed.

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CHAPTER 8

The Specific Influences of Nonspecific Effects

Mark D. Bishop and Joel E. Bialosky

Changes in the intensity of pain reported after any intervention are related to three general categories of effects: (1) condition-related factors, (2) the specific effects of treatment, and/or (3) nonspecific (treatment contextual) effects [19] (Fig. 8-1).

1. **Condition-related factors** refer to the biological aspects of the condition with which a patient presents and might include the natural course of the condition. Another condition factor is regression to the mean. This refers to the phenomenon in which a patient most often seeks care when the condition is at its worst and therefore likely to improve because of natural fluctuation or variation in the condition itself.
2. **Specific treatment effects** are the unique effects associated with the "active" ingredient of the treatment. For example, manual therapy interventions for pain such as joint mobilization and spinal manipulation impart well-established mechanical forces to the joint [25] and potentially result in improved clinical outcomes because of some corresponding changes in the mechanical properties of the targeted region [42].
3. **Nonspecific (contextual) factors** that comprise the **placebo effect** (and it is negative, nocebo) are inherent in all interventions for pain. Placebo effects/mechanisms have traditionally been conceptualized (negatively in many patients) as an inert part of treatment that is fake or passive, requires deception, and should be minimized or avoided. However, as we will describe, placebo is an active cortical mechanism that accounts for many treatment effects. In general, placebo effects are part of interventions for many conditions and these effects work through several different neurobiological mechanisms. Benedetti [2] indicates that many of these mechanisms activate receptors that also are the

binding sites for medications used in conditions ranging from Parkinson disease to depression. Placebo administration to patients with Parkinson disease, for example, causes dopamine release in the striatum and changes in basal ganglia and thalamic neuron firing [5]. Thus a central "pharmacological" mechanism can be activated by the central nervous system (CNS) in response to this "nonspecific" aspect of intervention.

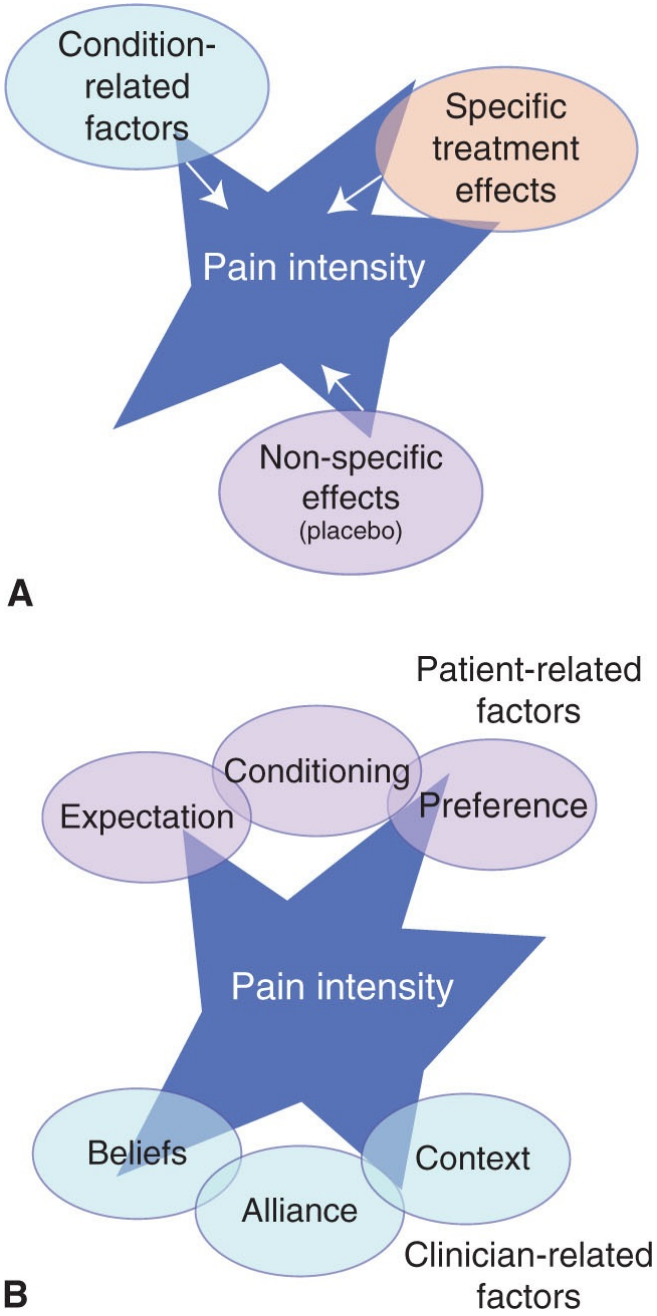

FIGURE 8-1 **A:** Diagram showing factors that can influence pain intensity. **B:** Schematic diagram showing nonspecific factors related to patient-related factors

and clinician-related factors that can influence pain intensity.

MECHANISM OF ACTION OF PLACEBO

With respect to pain, studies have demonstrated that placebo effects can be reversed by naloxone (an opioid antagonist) [1]. These studies suggest, therefore, that analgesia experienced in response to a placebo intervention involves activation of patients' own endogenous opioid pathways. Additionally, studies have shown that a placebo effect can be localized to a single body region [4] indicating that any placebo analgesia experienced is very specific, rather than simply a generalized release of opioids body- or CNS-wide.

Imaging studies confirm activation of regions involved in opioid analgesia, including the prefrontal cortex, the anterior cingulate cortex, and the periaqueductal gray and medulla using both positron emission tomography (PET) and functional magnetic resonance imaging (fMRI). For example, one study using fMRI demonstrated that when a patient experiences placebo-induced analgesia, the brain-related changes in pain processing were similar to those seen with opioid drug administration [16].

The opposite can also occur; that is, a worsening in a condition in response to potential bioactively inert agent—the **nocebo effect**. Less research has been devoted to the nocebo effect than to placebo. However, cholecystokinin (CCK) has been shown to play a key role in nocebo hyperalgesia of pain, likely through anticipatory anxiety mechanisms [3]. So, both placebo and nocebo effects are engaged and work through a patient's own internal pain system.

It may assist to rethink both the placebo (and nocebo) responses as endogenous, and therefore personal, modulatory mechanisms. The modulatory systems include expectation of the patient [7,8], equipoise (beliefs) of the practitioner [14,15], and treatment contextual factors such as the setting in which an intervention occurs and therapeutic alliance between provider and patient [21]. All of these factors separately and in combination can be decisive in treatment outcomes.

PATIENT-RELATED FACTORS

Expectations

Expectations can be categorized as an individual's belief of what will occur, what they desire to occur, or what they believe should occur [41]. We will focus this chapter on expectations as an indicator of what an individual believes will occur as these are known to influence pain response.

Patient expectations may influence the response to treatment and at times supersede the specific effects of treatment. For example, Kalauokalani et al. [27] randomly assigned 135 participants with low back pain to receive acupuncture or massage. Group-related differences in the primary outcome (disability per the Roland-Morris score) were not observed over the 10 weeks of the study; however, participants with greater expectations for acupuncture receiving acupuncture did significantly better than those with greater expectation for acupuncture receiving massage and vice versa. Additionally, Linde et al. [32] performed a pooled analysis of four randomized controlled trials of 864 participants with migraine, tension-type headache, chronic low back pain, and osteoarthritis of the knee, receiving either acupuncture or sham acupuncture over 8 weeks. Both acupuncture and sham acupuncture were associated with greater improvements in participants with high expectations for acupuncture, with an odds ratio approximating 2. Finally, Bishop et al. [8] performed a secondary analysis of 140 participants with neck pain, randomly assigned to receive spinal manipulation or exercise. At 1 month, a significant association was observed between improvements in the global rating of change score (i.e., "I feel much improved") and the general baseline expectation of "complete relief." Collectively, these studies support expectation as a key element for interventions for pain conditions.

In clinical practice, nonspecific treatment effects such as expectation may enhance or negate the specific effects of interventions for pain. A particularly elegant approach to assessing the influence of expectation on pain-related outcomes is the "open/hidden" paradigm. In this design, medication is provided by a medical provider either (1) in view of the patient or (2) through a hidden infusion in which the patient is not aware they are receiving medication. Studies using this methodology have observed significantly greater pain relief when patients are aware of having received a medication than when the exact medication is provided in a hidden manner [13]. Schenk et al. [37] observed lidocaine was more effective when it was given with an expectation of benefit than when it was given without an expectation of benefit or when placebo was given with the expectation of receiving lidocaine. Subsequently, nonspecific effects of treatment such as expectation may be additive to the specific effects of treatment serving to enhance the magnitude of observed outcomes.

A similar effect was noted in patients with irritable bowel syndrome (IBS)

undergoing rectal distension. When these patients were given oral lidocaine, rectal lidocaine, or rectal placebo, they were told, “The agent you have just been given is known to significantly reduce pain in some patients.” When the rectal nocebo condition was being tested, patients were told, “The agent you have just been given is known to significantly increase pain in some patients.” During the natural history condition, they would receive no treatment. In Fig. 8-2, it can be seen that the nocebo condition resulted in slightly higher pain ratings during the procedure and during testing of the skin. The placebo condition resulted in the same relief as oral and rectal lidocaine [44].

In sum, studies like this indicate that a patients’ expectation for benefit from a particular intervention must play an important part in the delivery and outcomes of that intervention. Francis Bacon was correct when he wrote that “what a man had rather were true, he more readily believes.” Although this statement was not related to interventions for pain but toward understanding of general phenomenology, it is pertinent and applies directly to those who seek our help.

So expectations of benefit seem to predict how patient’s respond to interventions. These expectations are generally very high among people who seek care. Intuitively this makes sense. You would not seek care if you didn’t think that there would be some benefit. But every one of us has worked with a patient who either does not think that you can help them or is only there in your office because “someone sent them.”

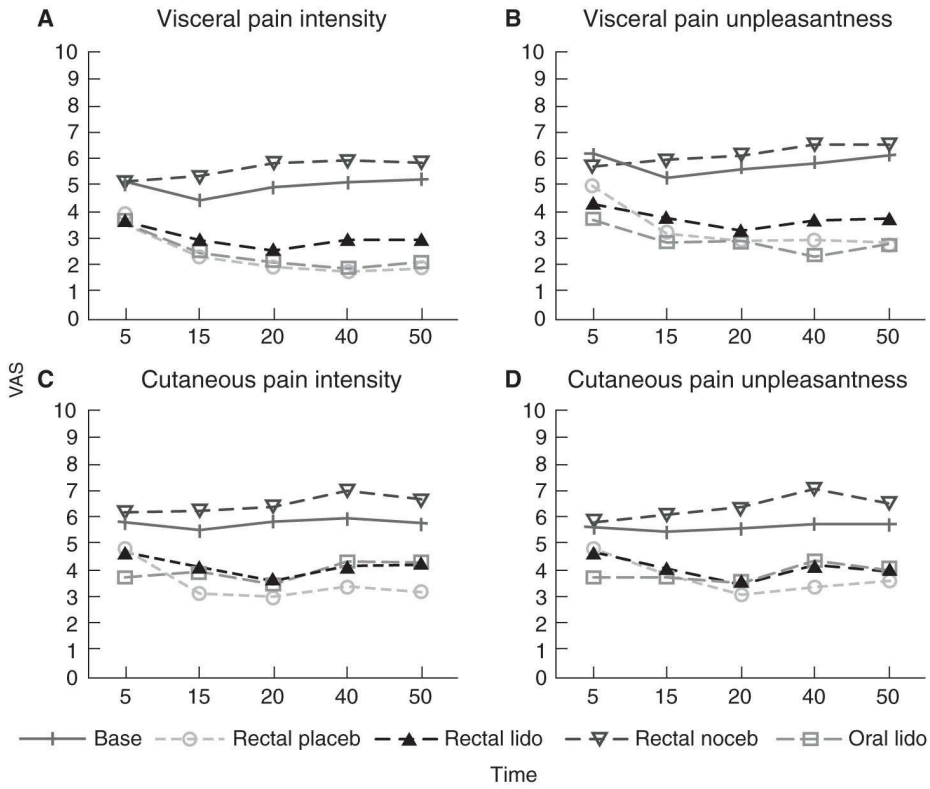

FIGURE 8-2 Comparisons of natural history (NH), rectal placebo (RP), rectal lidocaine (RL), oral lidocaine (OL), and rectal nocebo (RN) mean VAS ratings on visceral pain intensity **(A)**, visceral pain unpleasantness **(B)**, cutaneous pain intensity **(C)**, and cutaneous pain unpleasantness **(D)** during the 50-minute session. (Reused from Vase et al. [44], with permission.)

What Other Factors Are at Play?

Conditioning

Another mechanism through which physical therapy interventions might work relates to classical conditioning. In classical conditioning, repeated associations between a neutral stimulus and an unconditioned stimulus (intervention) result in the ability of the neutral stimulus by itself to elicit a response that is characteristic of the unconditioned stimulus. The placebo response can be conditioned under experimental laboratory conditions where pain is rated to a noxious testing stimulus. One method consists of surreptitiously lowering the temperature of the noxious testing stimulus following the administration of a placebo. When the temperature of the testing stimulus is returned to its baseline level after several conditioning trials, greater placebo hypoalgesia is observed [34].

Possibly one of the best examples related to physical therapy practice is the generation of similar pain experienced by the patient not tolerated in their daily activities, but now experienced as a result of an intervention (mobilization of a painful spinal level or performance of a stretching exercise). This painful intervention is now in the context of a safe therapeutic experience and is thought to change the way in which a patient views his or her pain. Some authors have also suggested that this effect might be based on theory of learning and pain memory [23,46].

Conditioning and expectations are very likely mixed together when we think of placebo effects in clinical practice [20]. Finniss et al. [20] suggest that expectations happen first, conditioning follows, and then everything depends on the success of that first interaction with the provider. This would mean that the first interaction is critical for the subsequent placebo responses: the higher the expectation, the greater the placebo effect, and, potentially, the greater the conditioning effects associated with a future intervention.

The patient's conditioned expectation is not only the result of the patient's personal experience [11], but may come from various sources of information such as the mass media or by observing the response of others [12]. For example, observation of an actor simulating responsiveness to a therapy resulted in placebo effects in subjects that were similar in magnitude to a classical conditioning protocol [12], indicating the presence of multiple placebo effects mediated by expectations and different types of learning.

Patient Preference

Patient preferences are those things desired by a patient during the therapeutic encounter (i.e., when they meet with you) and may be characterized as his or her preferred (1) role in the patient–provider interaction, (2) type of treatment, and (3) characteristics of the treating therapist (i.e., male or female, younger or older) [39]. These preferences for a specific type of intervention are associated with improved outcomes in individuals with musculoskeletal pain complaints [33]. Furthermore, compliance with any intervention may be improved when individuals are matched to interventions for which they have a preference [38]. What we are suggesting is that if a patient has a preference for one of two interventions that are equally beneficial, we should employ the one he or she prefers to gain the greatest treatment effect.

However, if you ask patients about whether they want to have a role in the clinical decision-making process, their response will be quite variable [35]. This suggests attention to preference should focus both on the patient's desired role

within treatment and upon treatment preferences for those wishing to participate. Patient preferences for a role in the clinical decision-making process vary by condition. For example, patients receiving treatment for cancer or undergoing invasive procedures are more likely to prefer participating in health care decisions than are patients with chronic conditions such as diabetes [9]. Furthermore, desire for involvement in the clinical decision-making process has increased over the years [9], suggesting patients currently desire involvement in this process more so than 10 or 20 years ago.

Lastly, an important area that is related is the manner in which the clinician's instructions about the entire rehabilitation process are presented to the patient. The art of communication has an incredible influence on outcome. We debated about whether or not this material was related more to patient expectation or therapeutic alliance (see section "Therapeutic Alliance" below). But we have included it here as the words you use mean everything. For example, 200 patients without a specific diagnosis were followed after a consultation with their general practitioner. Positive consultations provided a diagnosis and expectation of rapid recovery (e.g., "This is probably a virus, you will recover in about 1 week"). Nonpositive consultation did not provide a diagnosis or expectancy of improvement (e.g., "This could be a virus and I am not sure how long it will last"). A significantly greater percentage of individuals receiving positive consultation got better than those receiving nonpositive consultation [40].

Similarly, patients report [43] less pain after an injection with instruction that the anesthetic will "numb the area so that you will be comfortable" versus "you will feel a bee sting." All together, these studies across a variety of health care professions indicate that how we speak and interact with our patients has a profound impact on (1) what they expect from the intervention and (2) the outcome of your interaction with that patient.

PROVIDER-RELATED FACTORS

Therapist Equipoise

Just as patients present with specific expectations and preferences, health care providers are also prone to expectations and preferences for treatment approaches. Clinical equipoise is the lack of a preference or uncertainty for treatment [15]. Clinically, different clinicians favor different treatment

approaches and provide interventions enthusiastically and with the expectation of success. This equipoise influences clinical outcomes. For example, one study randomly assigned 149 participants with low back pain to receive either thrust or nonthrust spinal manipulation [14]. Neither group differed in terms of pain or disability upon discharge from the study; however, a significant relationship was observed between equipoise and clinical outcomes. Subsequently, clinician preferences and enthusiasm for an intervention may influence the corresponding outcomes.

Clinician beliefs other than equipoise may also influence clinical outcomes. For example, baseline physician expectations are predictive of response to acupuncture in individuals with chronic pain [45] and return to work following an acute episode of low back pain [28]. Whether consciously or subconsciously, provider beliefs influence how providers interact with their patients. Also, in a randomized controlled trial of chiropractic care for temporomandibular pain, one chiropractor delivered both the active intervention and the placebo intervention. Despite training to ensure consistent delivery across the groups, participants receiving the active intervention received more communication regarding clinical information or explanations, more directions and instrument thrusts, more optimistic or neutral statements, and longer treatment sessions [36]. Collectively, these studies suggest provider beliefs and expectations influence treatment outcomes related to pain conditions.

We have established that what you say and how you say it influences the response of your patient to an intervention, be it medication, surgery, or an intervention applied by a physical therapist. However, it is not just about what you say but also about the extent to which you believe what you are telling your patients. This therapist-effect is extremely powerful in all therapeutic interventions. The therapist's enthusiasm, language used, confidence regarding the beneficial effects of the technique used, and the like have powerful effects [24]. This means that clinician expectations about the intervention they are providing can influence outcomes.

Therapeutic Alliance

The relationship between the provider and patient can impact treatment outcomes. A warm, friendly, reassuring interaction is more effective at helping outcomes than an impersonal or uncertain interaction [17]. Examples include a study in which sham acupuncture effects were enhanced when provided in a way that improved therapeutic alliance [29] and another that showed that interferential electrical stimulation was significantly more effective in alleviating

pain when provided in a “warm and welcoming, manner to enhance therapeutic alliance” [21] compared with a neutral patient–therapist interaction. Results of this latter study are presented in Fig. 8-3, where it can be seen that the effects of the placebo intervention were also increased by an enhanced therapeutic alliance.

In order to maximize placebo effects, therefore, physical therapists are encouraged to minimize the patient’s negative mood and thoughts regarding the pain condition and to draw on patient preferences and past experience for evidence-based interventions [6]. Spending more time with patients explaining their condition is essential for enhancing outcomes, as this reduces the patient’s emotional distress. We propose that pain education provides an explanation for their pain, explains the possible treatment strategies, maximizes realistic expectations, and establishes a good therapeutic alliance [18]. The main ingredients of the therapeutic alliance are the patient’s ability to forge a bond with the clinician and the clinician’s ability to present his or her self as caring and sensitive.

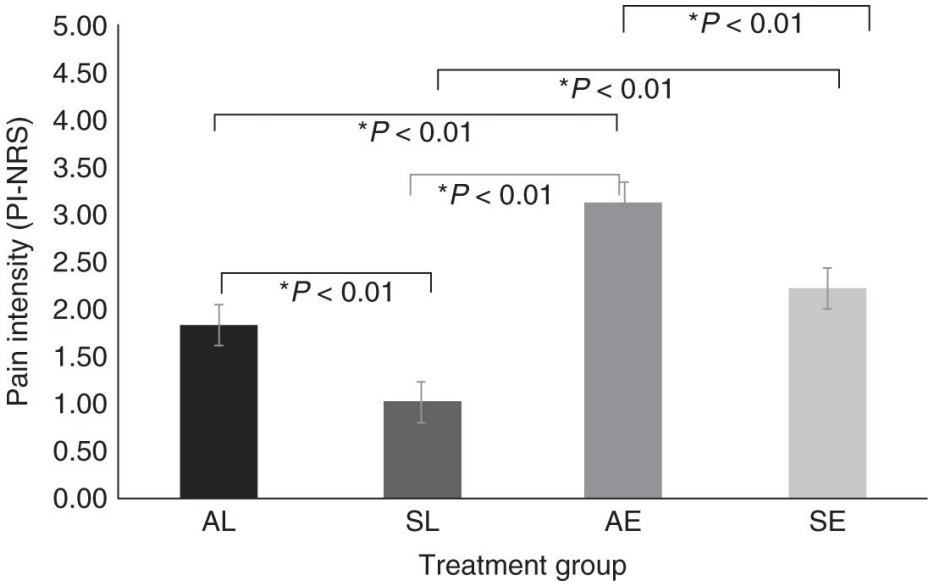

FIGURE 8-3 Between-group differences for pain intensity scores. Results are shown as mean ± SE of measurement. The AL group received active interferential current therapy (IFC) combined with a limited therapeutic alliance (TA), the SL group received sham IFC combined with a limited TA, the AE group received active IFC combined with an enhanced TA, and the SE group received sham IFC combined with an enhanced TA. PI-NRS, pain intensity numerical rating scale. Asterisk indicates significant at $P < 0.01$. (Reused from Fuentes et al. [21].)

Context

The context in which the intervention takes place also has considerable effects. This is a less studied area of patient expectations, but intuitively most of us know what this is. When you go to a provider, you expect certain things to happen. When I go for an annual physical, I expect to wait for a while, be seen by medical assistant to have my vitals taken and be taken back to a room to wait. These factors also influence patient receptiveness to the clinician's instructions, the interaction between the clinician and the patient, and the intervention the clinician and patient finally agree upon. These particular types of expectations relate to satisfaction with the delivery of care [22].

CLINICAL IMPLICATIONS

It is essential to consider the patient's expectations and preferences when choosing an intervention. A standardly recommended measurement tool for expectation or preference does not exist, so in the absence of such a tool, we suggest using simple numeric rating scales. Expectation is more closely aligned to clinical outcomes when they are specific to an outcome and a time frame [26]. For example, "What do you expect your pain to be, following 3 weeks of physical therapy? 0 = *no better or no preference* to 10 = *completely better*." Or "How do you expect you will be able to perform the lifting required for your usual job performance, following 3 weeks of physical therapy? 0 = *not be able to perform*; 10 = *completely able to perform*." Realize that expectations and preferences may apply to different factors. Patients may have general expectations or preferences for treatment such as seeing a physical therapist or a surgeon. Alternatively, patients may have specific expectations or preferences for treatments such as massage versus exercise. Or patients may have greater expectations for treatments such as surgery when compared with exercise. Finally, patients may have expectations or preferences for the provider, such as expecting better success if they see the physical therapist recommended by their physician or preferring a female physical therapist over a male. The effectiveness of an intervention may be enhanced when, on the basis of the evidence of the effectiveness of that treatment, patient expectation is increased in view of the possibility of a positive response to treatment. Alternatively, outcomes may worsen on the basis of the interaction between the patient and therapist.

To summarize,

1. Be confident as your own expectations may enhance your outcomes.
2. Build rapport as better therapeutic alliance may improve your outcomes.
3. Check on what has worked in the past for patients as patients may have been conditioned to expect improvement from specific interventions.
4. Check on what the patient wants as patients may have higher expectations or preferences for specific interventions.
5. Realize prior negative experiences with treatment correspond to less effective interventions [30].
6. Realize failure of a current treatment to meet expectations can result in lack of response to future interventions [11].
7. Clinicians may be prudent to consider whether patients have not responded previously to an intervention and to maximize realistic expectations for current treatments to ensure expectations are met.

Some readers may be thinking that they don't what to engage an "active cortical effect" (placebo) in their interventions and they "only use interventions based on evidence-based practice." What if the evidence says that some of what we do well doesn't happen in the periphery where our interventions are directed but happens in the cortex? Does that make it less important? How do I responsibly use an intervention that includes a placebo effect?

A primary concern about the use of placebo clinically is the ethical implications of deceiving a patient. Although not systematically studied, preliminary indications are deception with the intention of helping is not harmful. For example, in one study participants with IBS reported no changes in attitudes about the likelihood of future medical use for pain, likeability and trust of the experimenters, or depression, anxiety, anger, or fear following disclosure of receiving a placebo. In fact, a slight improvement was observed in frustration. These findings suggest no adverse effects occur in patients aware of having received a placebo [10]. Furthermore, a survey of individuals with chronic musculoskeletal pain conditions found participants did not mind receiving the placebo intervention if they experienced pain relief [31]. Subsequently, engaging or enhancing the placebo effect for the sake of helping a patient seems to be well tolerated and acceptable—particularly, if the patient benefits from the intervention.

One very interesting development with implications related to the "ethics" of using interventions that include enhancement of these nonspecific effects is the

finding that deception is not necessary to induce a pain-relieving response. For example, a recent study used “open labeled placebos” with patient education that described an active biological pathway for symptom improvement; that is, participants were told that they were receiving a placebo treatment—investigators told patients with IBS that they would be randomized to receive either a placebo sugar pill or no treatment [29]. The participants who got the placebo pill were told that placebos have been found to produce clinically effective results through a mind–body connection and that by taking the pill, they would be harnessing their own recuperative powers. Greater clinical improvement was found in the placebo group compared with the no-treatment group. These findings suggest education about the influence of cortical effects upon the pain experience may be beneficial in and of itself.

None of the previous paragraphs are intended to suggest that clinicians currently, or should in the future, use placebo interventions—far from it. What we are suggesting is that knowledge of how to enhance nonspecific effects of any intervention may be of great benefit to our patients.

So how do we put it all together? Here is our advice. First, ask the patient if there is anything that has worked in the past or anything he or she thinks will work now. Next, find out what it is exactly that the patient expects from the interaction. Work to develop a management plan on which you and your patient can agree. Last, be sincere, be positive about your plan, and let patients know that you care.

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CHAPTER 9

Education and Self-Management for Pain Control

Kathleen A. Sluka and G. Lorimer Moseley

Patient education and self-management are standard of care for any health-related condition and have become essential for chronic diseases. Nearly all clinical practice guidelines for chronic diseases include a recommendation for education and self-management. Self-management programs encourage people with chronic diseases to take an active role in the management of their condition and aim to support ongoing medical care. For chronic pain conditions, self-management programs are supplemental to an interdisciplinary plan of care.

Self-management programs are quite variable and can include a variety of different components. Common components of a self-management program include (1) patient education on pain and disease; (2) education on increased movement, activity, and pacing; (3) development of pain-management skills with nonpharmacological approaches; and (4) development of coping skills. Self-management programs can also be delivered in many formats, including individualized, group, or combined sessions and single or multiple sessions, or by trained health care practitioners (nurse, physical therapist, physician, psychologist) or non–medical-trained facilitators. Information can be delivered verbally, in written form, and/or through multimedia, the Internet, and technology strategies.

For chronic pain, self-management is a structured multicomponent intervention. Again the main goal is to provide resources and skills to the patient for them to more effectively manage their chronic pain. Importantly, self-management skills for those with pain are part of a comprehensive plan of care that would include medical management, physical therapy management, and potentially psychological interventions. All practitioners educate and provide self-management skills that are generally complementary to each other. Through self-management and education, we aim to make the patient an active participant

in the management of their condition—give him or her the skills to master his or her own situation—and, as such, often times are expecting behavioral changes. As such if education and self-management interventions are expected to have a long-term effect, we must make sure that people not only understand the material, but also change their behavior. For example, everyone knows already that exercise is good for themselves and that being overweight is not healthy. However, we have a society that is sedentary and overweight that continues to increase in proportion. Therefore, the role of the clinician is as the guide or coach and the patient is the student. We provide problem-solving and decision-making skills so the patient can engage in an active program.

Physical therapists are ideally suited to deliver self-management programs. They spend significant time interacting with their patients through delivery of a variety of treatments and have a solid grounding in biological sciences. Physical therapists' knowledge of pain sciences in particular is also rapidly increasing: 15 years ago, most health professionals had a poor understanding of the biology of pain but physical therapists demonstrated an advanced ability to take on new information [32]. A recent reappraisal of the state of the field shows substantial improvement in pain science knowledge in physical therapists from numerous countries [26]. This widespread upgrading of pain science knowledge is reflected in the proliferation of professional development courses targeting pain-related knowledge (e.g., "explaining pain"; see reference [37] for review).

This newfound advanced level of pain science knowledge complements the physical therapists' wider knowledge and skill set—a good understanding of the components of self-management programs, including concepts of presentations and progression of disease, principles of movement, exercise, graded exposure, recovery, and use of nonpharmacological therapies to offer real-time analgesic and motivational benefits. Furthermore, physical therapists are often one of the first providers to treat people with acute and chronic pain and, in many countries, are first-contact practitioners and a key primary care provider. Indeed, there are a number of recent studies that train physical therapists to deliver education and self-management approaches, including the principles of cognitive behavioral therapy. This chapter will review the different types of self-management and education approaches available and the clinical evidence for their effectiveness in the treatment of individuals with chronic pain, particularly as they pertain to the practicing physical therapist. However, what is outlined is important for all practitioners, regardless of discipline.

SELF-MANAGEMENT PROGRAMS

The following are a series of components that are included in a self-management program: (1) patient-appropriate education and health literacy upskilling. For those with pain, which is the vast majority of those with chronic disease, this would include information on the biological processes underpinning pain—so-called explaining pain [2,37]—but also include disease-specific education. For those with fatigue, depression, or anxiety, similar approaches to "explaining fatigue" can be utilized. Health literacy training aims to provide the person with pain with the following:

1. Fundamental skills to negotiate the health care system and environment;
2. Advice, training, and motivation to adopt an active lifestyle and to exercise; and
3. Advice, training, and motivation on pacing activities based around managing pain and other symptoms, and response to activity.

This would include a collaborative approach to identifying key behavioral goals and strategies with which to achieve them; 2) The principles of graded exposure and pacing and strategies to optimize sleep 3) Training and resources in self-administered strategies that target stress reduction and pain relief such as relaxation therapy, mindfulness, massage or therapeutic movement and motor imagery [38] (Chapter 16) 4) Training in other analgesic strategies that the subject can use to modulate their pain and other symptoms, for example over-the-counter medications (note that upskilling of health literacy is particularly important here), heat, cold or TENS.

All self-management plans need to be patient specific and be established within a truly collaborative framework—one in which the person with pain is key in developing goals and outcomes. Goals need to be realistic and outcomes need to be in line with what the person with pain wants. This is not a trivial consideration because most people in pain initially have a clear goal of being pain-free—after all, that is arguably the biological purpose of pain—to compel the sufferer to get out of pain and thus out of danger. Yet for many people in chronic pain, this is not a realistic short-term or medium-term goal. The clinician must therefore pay special attention to helping the person in pain shift his or her understanding of his or her own "biological situation" and work with him or her toward establishing attainable goals on the basis of different frameworks, for example, values-based [57], work-based, or leisure-based [40] frameworks.

Regularly modifying goals and giving people in pain the skills to modify and update their own goals will optimize the likelihood that they will in fact gain mastery over their situation and develop a sense that they themselves are in control, rather than other people or factors being in control of them (see references [5,12,22] for early work on these concepts). Ideally, the collaboration between the clinician and the person in pain leads to the development of an active management plan, with clear, achievable, and modifiable goals and a suite of accessible resources, strategies, and skills that lessen the impact of pain on functioning and quality of life. This plan will include what to do if pain gets worse and what to do as pain gets better. Although this overlaps with pacing, it is important to recognize that there will always be bad days and good days and one must use each of these as a learning event. To get people to write out their plans and to individualize these plans will help give them control over their health and quality of life.

EDUCATION

Education is one component of self-management programs and can be broadly categorized as education related to biology and pathology and education related to behavior and skill. With respect to chronic pain, the former is most easily characterized as “explaining pain” (EP). Ever since EP was first tested in a randomized controlled trial (RCT) [30], it has evolved and been adapted, for example, as small-group tutorial-type sessions, or large-group seminars lasting up to 3 hours [31–34,39,41,50]. Other research groups have adapted the content for related conditions (e.g., chronic fatigue syndrome, fibromyalgia, and postsurgical pain) [25,29,54,55], and others have integrated the material into text-only interventions [53] or story books [10]. Common to all these approaches is the core objective of shifting understanding of the biological processes that underpin pain and the effects of neuroplasticity on those processes; to gain a “functional pain literacy” [37]. That is, they gain a current understanding of how pain is produced, why pain can persist when tissues are healed, and how pain can be seen as a truly biopsychosocial phenomenon. They can integrate this new understanding into their wider pain and function-related beliefs, their attitudes, behaviors, and management plan including lifestyle and work- and leisure-related choices [37].

Conceptual Framework

EP is based on a modern understanding of pain that emphasizes its protective function rather than it being a marker of the state of the tissues. A vast body of empirical data shows that a wide range of variables—physical, cognitive, emotional, and environmental—can modulate pain (see reference [2] for one accessible and comprehensive account). Rather than commit to memory the various effects, it is much easier to understand the principle that governs the modulatory effect of these variables: information that signals danger to body tissue stands to increase pain and information that signals safety to body tissue stands to decrease pain [37]. From a neurological perspective, the modality of the information being evaluated by the brain is not critical. Nociceptive input provides the most obvious and perhaps potent information about danger to body tissue and is widely held to be “hard wired” such that noxious stimuli evoke protective responses and enhance subsequent protective responses even in newborns [49]. However, otherwise benign contextual cues, such as red or blue lights, can have profound influences over the intensity of pain evoked by noxious and non-noxious stimuli [35].

The potential impact of gaining a new way of understanding pain is further enhanced when patients understand the normal adaptations that occur within their bodily systems when pain persists. New information is best presented skillfully, respectfully and with a “coach” mentality rather than a “healing” mentality [23]. Learning goals include: persistent pain is associated with central sensitization, facilitation of the neural mechanisms that underpin pain and other protective outputs, a sometimes “vicious cycle” of threatening inputs, producing protective responses, which in turn evoke threatening inputs (see reference [2]). Achieving these goals can offer profound reassurance to people in pain because it fundamentally shifts the meaning of their pain. That pain is itself fundamentally dependent on meaning implies that undergoing that conceptual shift will lead to lower pain because the reason to protect is reduced. This theoretical prediction is now supported by a series of studies showing immediate effects [39,54] and clinical trials (see below). That education about pain can be reassuring is not a new concept [52], but the substantial progress that has been made in the integration of conceptual change theory and principles of multimedia learning into pain-related education has revealed an effective therapeutic intervention—EP—on the basis of changing how people think about their pain.

Although EP is now considered best practice and recommended in clinical guidelines for the management of pain in some countries (e.g., National Pain Strategy, Painaustralia, 2010), it is still sometimes mistaken for conventional pain education components of self-management and pain management programs.

Differentiating the two is important because EP focuses on *why* to take a graded exposure-based, pacing-based, and biopsychosocial approach to rehabilitation, whereas conventional education has focused on *how* to take that approach. This has been discussed at length elsewhere [37]; in brief, as long as the person in pain links his or her pain to tissue damage, the idea of pacing, graded exposure, and implementing strategies that do not train, repair, or strengthen that body part makes no sense. One might predict that, without reconceptualizing pain, a self-management approach is unlikely to succeed. For this reason, we would see EP and facilitating the adoption of a "protect from bodily danger" paradigm of pain to be a cornerstone of self-management, arguably providing the necessary platform on which the remainder is built. Self-management programs by definition do not seek repair, ablation, or denervation of injured tissue, but rather they seek to provide the person in pain with mastery over his or her pain or disease and meaningful engagement in life. People can learn to practically apply this paradigm to their situation through simple tools such as the Protectometer [36], a practical method of facilitating the shift to a truly biopsychosocial understanding of pain as one part of a wider protective system incorporating other bodily outputs, for example, motor or autonomic outputs [37]. Clinicians also now have access to a wide range of resources to increase their own knowledge of pain science and their proficiency in educating their patients and, indeed, the wider community in a "preemptive" manner.

Education related to new behaviors and pain management skills is integral to self-management and is mostly discussed at length below. One additional component is that of increasing general health literacy skills. This material is reasonably generic and includes giving people principles to guide their interaction with clinical providers, for example, writing down questions for their clinician before they visit, including "the big four": What is wrong? What can you do to help? What can I do to help? and How long will it take? [38]. Other examples include how to understand dosages, how to fill out forms, and what information should be disclosed in the interests of accessing optimal care, availability of transport, social work assistance, and occupation-related obligations and responsibilities. The resources that are required to negotiate a typical health care system are taken for granted by many of us—arguably all those reading this chapter—but there is compelling evidence that the wider community has very low health literacy levels and that low healthy literacy is strongly associated with poorer health outcomes across conditions and jurisdictions [18].

Relaxation and stress management skills are key components of a self-management program. Relaxation interventions use many different techniques

and include progressive muscle relaxation, rhythmic breathing, and autogenic training [20]. Systematic reviews show weak evidence for the effectiveness of relaxation techniques with the most evidence for progressive muscle relaxation for a variety of chronic and acute pain conditions [20,28,46]. All of the reviews caution the findings as these studies typically have significant methodological issues and small sample sizes.

Pacing is also a key component of educational programs and focuses on training an individual to monitor, adjust and pre-plan activity levels and combinations so as to avoid flare-ups. Avoidance of activity is consistently associated with more pain and disability. Surprisingly, pacing on the other hand is generally linked with better psychological functioning but more pain and disability [1]. A systematic review in people with osteoarthritis identified 1 trial with 32 participants and showed a positive effect on joint stiffness and fatigue that is more effective when tailored to the individual [48]. Clearly, further studies are needed to more fully evaluate the value of adding pacing to a self-management program.

Coping strategies and problem-solving training are generally included in education and self-management programs, in addition to cognitive behavioral therapy commonly employed by psychologists (see Chapter 16). These strategies will be discussed in more detail in Chapter 16, but these techniques have recently been employed by physical therapists and are common parts of a comprehensive self-management and education plan of care.

Pain-Relieving Modalities

Teaching people with acute and chronic pain the appropriate methods for using heat and cold can provide a mechanism for subjects to control their pain without the use of medications. These types of modalities provide temporary relief of pain that can be invaluable to a person with a chronic pain condition and provide an alternative to ongoing pharmacotherapy. Additionally, instructing and providing subjects with a TENS unit for home use can also provide an additional pain-relieving alternative to pharmacotherapy for people with chronic pain. Although these are considered passive treatments, the use of these treatments in self-management provides the person with pain a method of self-management that may change the locus of control. Subsequent chapters will review the evidence, both clinical and basic science, for a variety of pain-relieving home care modalities (Chapters 11 and 12).

CLINICAL EFFECTIVENESS FOR EDUCATION AND SELF-MANAGEMENT

Several RCTs have examined the effectiveness of EP and self-management approaches on chronic pain conditions. Table 9-1 summarizes the relevant systematic reviews in a variety of acute and chronic pain conditions. Inherent in the clinical literature is the heterogeneity of the self-management programs, poor methodological quality of the trials, and lack of an appropriate placebo control group. In general, most studies examining education and self-management compare to usual care, or wait-list control groups, and comparisons are generally assessed at short-term after the intervention. Few long-term follow-ups have been done.

Self-Management Programs

Several systematic reviews report negative or inconclusive findings for effectiveness of more conventional, structural pathology–based education and self-management programs for acute or chronic pain conditions: osteoarthritis, low back pain (LBP), chronic musculoskeletal pain, chronic pain, chronic LBP, and chronic neck pain. As an example, a recent Cochrane systematic review examined effectiveness of self-management in people with osteoarthritis. They included 29 trials with 6743 participants. Data analysis shows that, when compared with usual care, there was a small effect on pain, function, and quality of life that is likely not clinically significant (<1/10 on pain scale). Furthermore, when compared with an attention control group there was no difference [19]. For individuals with subacute LBP a single 2.5-hour oral session was effective in return to work, and for those with acute whiplash there was a positive effect [8]. However, for chronic back and neck pain, individual education sessions are not effective [8]. In most cases, the quality of the studies was very low and thus the systematic reviews caution against the conclusions.

Interestingly, a recent systematic review shows use of technology-assisted self-management (e.g., Internet-based or iPhone apps) to assist in self-management show improvements in pain [8]. It may be that more recent studies employ different or more comprehensive approaches to education and self-management. For example, traditional back schools focusing on the biomedical model found that studies were either mixed or ineffective. On the other hand, education that employs a more biopsychosocial and interdisciplinary approach

may be effective for some conditions (for review, see reference [27]). For example, in people with OA and spinal pain, Jordan et al. [17] show that self-management programs improve exercise adherence (N = 42 studies, 9243 participants), which may be particularly important for physical therapy. Similarly, RCTs show applying self-management, education, motivational interviewing, or hypnosis together with physical therapy can enhance adherence and effectiveness of exercise in people with chronic pain conditions (LBP, fibromyalgia) [3,43,56].

Explaining Pain

The efficacy of explaining pain has been tested with RCTs in cohorts with chronic LBP [30,32,39,41,44], lumbar radiculopathy [25], chronic fatigue syndrome [29], whiplash [55], fibromyalgia [53,54], and people with a range of chronic pain disorders [10]. Systematic reviews have been conducted and they draw reasonably similar conclusions. A particularly liberal systematic review [24] that set a low bar for methodological quality of included primary studies made very positive conclusions—that there is good evidence that EP decreases pain, increases physical performance, decreases perceived disability, and decreases catastrophization. The other, more conservative, review was unsurprisingly more measured [4], concluding low-level evidence for EP as a stand-alone intervention to improve pain or disability. Since these prior systematic reviews, the literature has been updated using systematic review protocols, a priori search terms, and inclusion and exclusion criteria [37] and includes the addition of four RCTs [10,41,53,54] with positive results. Nonetheless, limitations of the evidence base remain (e.g., most studies are small) and although patients can be blinded to the hypothesized effect of interventions, clinicians cannot.

TABLE 9-1 **Summary of Effectiveness of Education and Self-Management Programs for Pain Control**

Intervention	Population	Number of Studies/ Participants	Type of Study [reference]	Comparison Groups	Results
Self-management skill and technique acquisition, health-directed activity, self-monitoring, and insight	OA	*N* = 29, 6743 participants	Cochrane review [19]	Compared with attention control, usual care, information alone, another intervention	Compared with attention control, no effect on pain, function QOL Compared with usual care, small effect on pain, function QOL that may not be clinically significant
Self-management to improve exercise adherence	CMP	*N* = 42, 9243 participants (OA and spinal pain)	Cochrane review [17]		Improvement in exercise adherence with self-management programs
Cognitive behavioral therapy through the Internet	Chronic pain	*N* = 15, 2012 participants	Cochrane review [6]	Cognitive behavioral therapy through the Internet	HA-reduced pain and disability Non-HA pain, disability, depression and anxiety
Education for LBP	Subacute and chronic LBP	*N* = 24	Cochrane review [8]	Compared with no interventions, noneducational intervention, other educational interventions	Subacute LBP: 2.5-h oral session more effective on return to work Less intensive not effective Individual sessions is effective on pain and global improvement Chronic: individual education less effective than back pain–specific function. No difference between different types of sessions
Group-based PT-led self-management interventions	OA and CLBP	*N* = 22	Systematic review [49]	Compared with individualized PT or usual care	*N* = 22, 10 OA, 12 CLBP—no significant difference between groups
Technology-assisted psychological self-management interventions	Chronic pain	*N* = 44	Systematic review [13]		Improvement in self-management and pain
Education	Acute and chronic neck pain	*N* = 15	Cochrane review [11]		Positive effect for acute whiplash-associated disorder; no evidence for subacute or chronic pain or disability
Neurobiology of pain education	Chronic LBP, chronic fatigue, chronic WAD	*N* = 8	Systematic review [24]		Reduces pain and disability
Neurobiology of pain education	Chronic LBP	*N* = 2, 122 participants	Systematic review [4]		Low-quality evidence of benefit for pain and function (0.5-mm difference on 0–10 scale)

Abbreviation: LBP, low back pain.

Notably, of course, EP is not intended to be a stand-alone intervention, but rather part of a wider self-management/rehabilitation approach. Moreover, like other interventions, EP requires the clinician to have certain competencies, most obviously a personal conceptualization of modern pain biology that is consistent with the current science. Current data suggest that most physical therapists are "at the leading edge" of understanding of pain science and integrating it into practice [26].

UNDERLYING MECHANISMS FOR EDUCATION AND SELF-MANAGEMENT

As discussed in Chapters 2 and 3, there are complex processes throughout the peripheral and central nervous systems that underlie the processing of pain, and these can result in more long-term alterations both peripherally and centrally in those with chronic pain. The underlying mechanisms for how education and self-management techniques reduce pain are unclear. However, recent research has begun to examine the underlying principles. Education and self-management are aimed at changing behaviors and patient beliefs. As such, changing these beliefs about pain could reduce distress, catastrophizing, and anxiety [27]. Changes in these beliefs are associated with clinical improvements [15] (Chapter 16). In particular, knowledge acquired during education predicts decreases in pain intensity and disability [16]. However, most clinical studies have not measured

patient beliefs, and thus it is unclear whether the conflicting clinical evidence for self-management programs is due to a failure to change beliefs or the ineffectiveness of the trial.

The mechanisms by which education (including explaining pain) and self-management improve in pain and disability could be through multiple biological pathways:

1. Primary modulation: direct modulation of the neural networks in the cortex that represent pain and other protective outputs
2. Secondary modulation: modulation of ascending nociceptive input by the activation (or reactivation) of descending inhibitory pathways, via midbrain nuclei such as the periaqueductal gray or rostral ventromedial medulla
3. Tertiary modulation: modulation of incoming danger cues as a result of downregulation of other protective systems; for example, modulation of nociceptive input directly, immune cell function, triggers for fear, increased movement, or altered behaviors (Fig. 9-1)

These three potential pathways are similar to that observed with cognitive behavioral therapy. Activation of the different mechanisms is not mutually exclusive. Rather, more than one of these may be occurring simultaneously or across time to modulate pain. Recent data have begun to examine these underlying mechanisms using a series of approaches including brain imaging, pain physiology measures (pain thresholds, conditioned pain modulation), and analysis of patient beliefs.

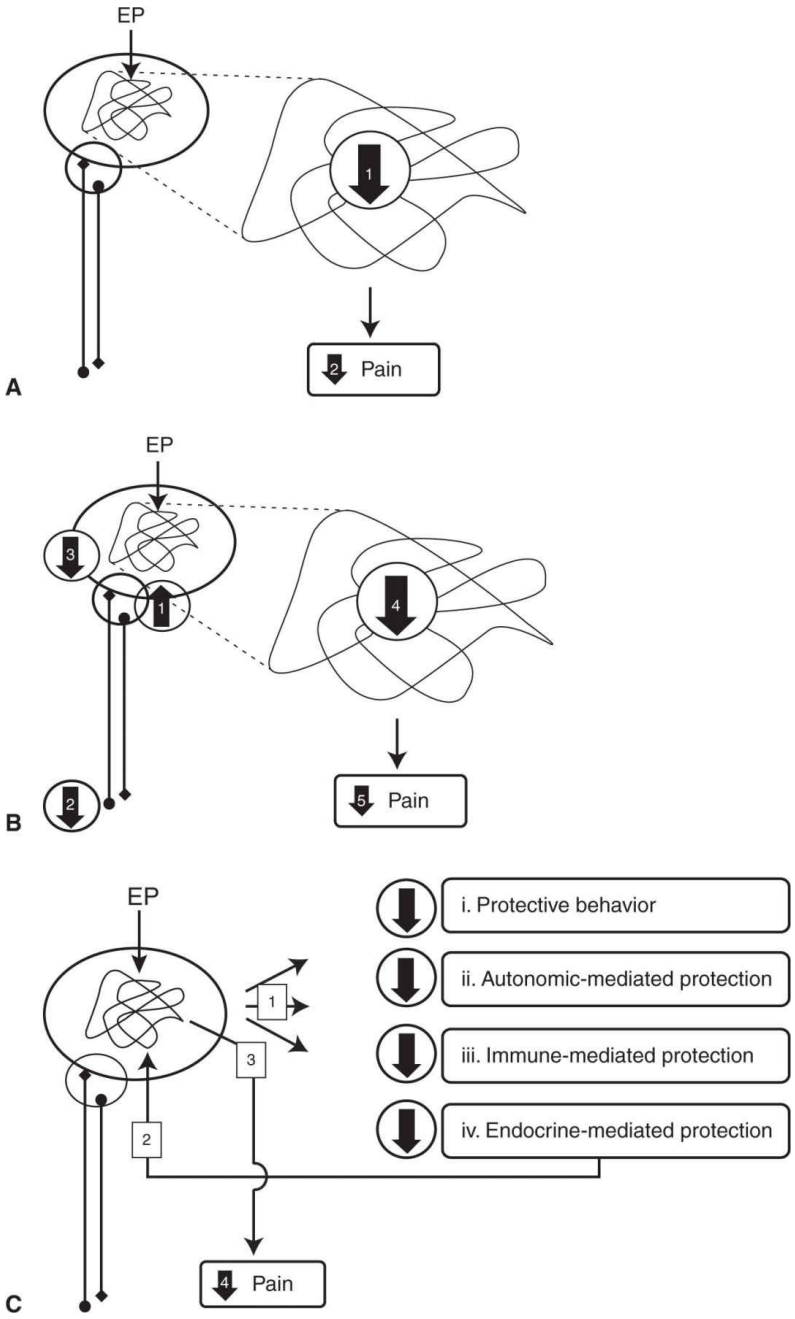

FIGURE 9-1 **A:** Primary modulation of pain by explaining pain (EP). EP changes the way in which incoming input is evaluated, decreasing activation of protective representations *(1)*, thereby reducing pain *(2)*. **B:** Secondary modulation of pain by EP. EP increases midbrain-mediated descending inhibitory output *(1)*, which decreases activation of the spinal nociceptor *(2)*, decreasing nociceptive input to the brain *(3)*, and activation of protective representations *(4)*, thereby reducing pain *(5)*. **C:** Tertiary modulation of pain by EP. EP downregulates other protective outputs, increasing "safe" behaviors (e.g., normal activities, exercise, and movement), broadly captured by increased self-

management *(i)*, decreasing autonomic activation *(ii)*, immune activity (e.g., inflammation) *(iii)*, and endocrine activation (e.g., cortisol release) *(iv)*. These shifts in other output systems necessarily shift the mix of information being detected and transmitted to the brain—so-called "interoception," thereby further decreasing activation of protective representations *(3)*, and thereby further reducing pain *(4)*.

Recent brain imaging studies show alterations in various cortical areas involved in processing pain after cognitive behavioral therapies (for review, see reference [9]) and are consistent with the first hypothesis. The cognitive behavioral interventions include education and self-management strategies outlined in this chapter. Specifically, in people with irritable bowel syndrome, cognitive behavioral interventions that include education, coping skills training, and problem solving improve pain and anxiety and also reduce activation in a number of cortical areas involved in pain processing, including the amygdala, anterior cingulate cortex, and frontal cortex [21]. A similar study in people with fibromyalgia (N = 43) revealed increased activation of the prefrontal cortex after treatment, and increased connectivity between the prefrontal cortex and the thalamus, suggesting a normalization of brain function with treatment [14]. Distraction in healthy individuals also reduced pain intensity ratings and altered activation of the anterior cingulate cortex, and a short cognitive behavioral treatment in healthy subjects reduced secondary hyperalgesia, a measure of central excitability [45]. In people with chronic pain, an 11-week cognitive behavioral intervention that targeted coping skills improved activity, exercise and pacing, and relaxation and imagery and significantly increased reduced gray matter volume. There were also clinical improvements in catastrophizing, quality of life, and depression, with pain catastrophizing correlated with increased gray matter volume after cognitive behavioral therapy [47]. Thus, therapies aimed at self-management and changing patient beliefs not only improve pain, disability, and quality of life but also normalize some of the abnormalities in brain structure and function that are associated with chronic pain.

It has become well established that pain catastrophizing is a predictor of poor outcome in a variety of clinical conditions [42]. Interestingly increases in IL-6 are also induced during painful stimulation in those with the highest levels of pain catastrophizing [7], suggesting that alterations in the immune system could be mediated by negative beliefs (Hypothesis 1). Thus, targeting techniques to reduce catastrophizing could have significant effects on cortical processing and systemic cytokine release.

For explaining pain, people with chronic low back and leg pain were randomly allocated to EP or explain spinal physiology and anatomy [33]. Immediately before randomization and immediately after the intervention, subjects were asked to rate the threat value of pain and their pain threshold during a straight leg raise. Those with an increased understanding of their pain had a matching increase in their pain threshold. That is, the cognitive intervention had a direct and immediate effect on pain threshold—consistent with the primary modulation pathway in Fig. 9-1A. People with fibromyalgia treated with explaining pain showed a rapid reinstatement of conditioned pain modulation, an effect that was not observed in those allocated to the control intervention [54], consistent with the secondary modulation pathway in Fig. 9-1B. The decreases in catastrophizing, increased sense of control and mastery, reduced fear, and increased acceptance might all operate via the tertiary modulation pathway (Fig. 9-1C).

Education and self-management techniques clearly activate and modulate multiple pathways at the cortical, subcortical, nociceptive, and even non-nociceptive levels (Fig. 9-2). These include areas such as the prefrontal cortex and anterior cingulate cortex and may also affect other regions such as the amygdala by reducing fear of pain and movement. These regions can then modulate the descending inhibitory pathways originating in the periaqueductal gray (PAG) and rostral ventromedial medulla (RVM) that project to the dorsal horn to modulate nociceptive input. Untangling the contribution of each pathway to reductions in pain would be very difficult; it is likely that each pathway contributes variably in an individually specific manner.

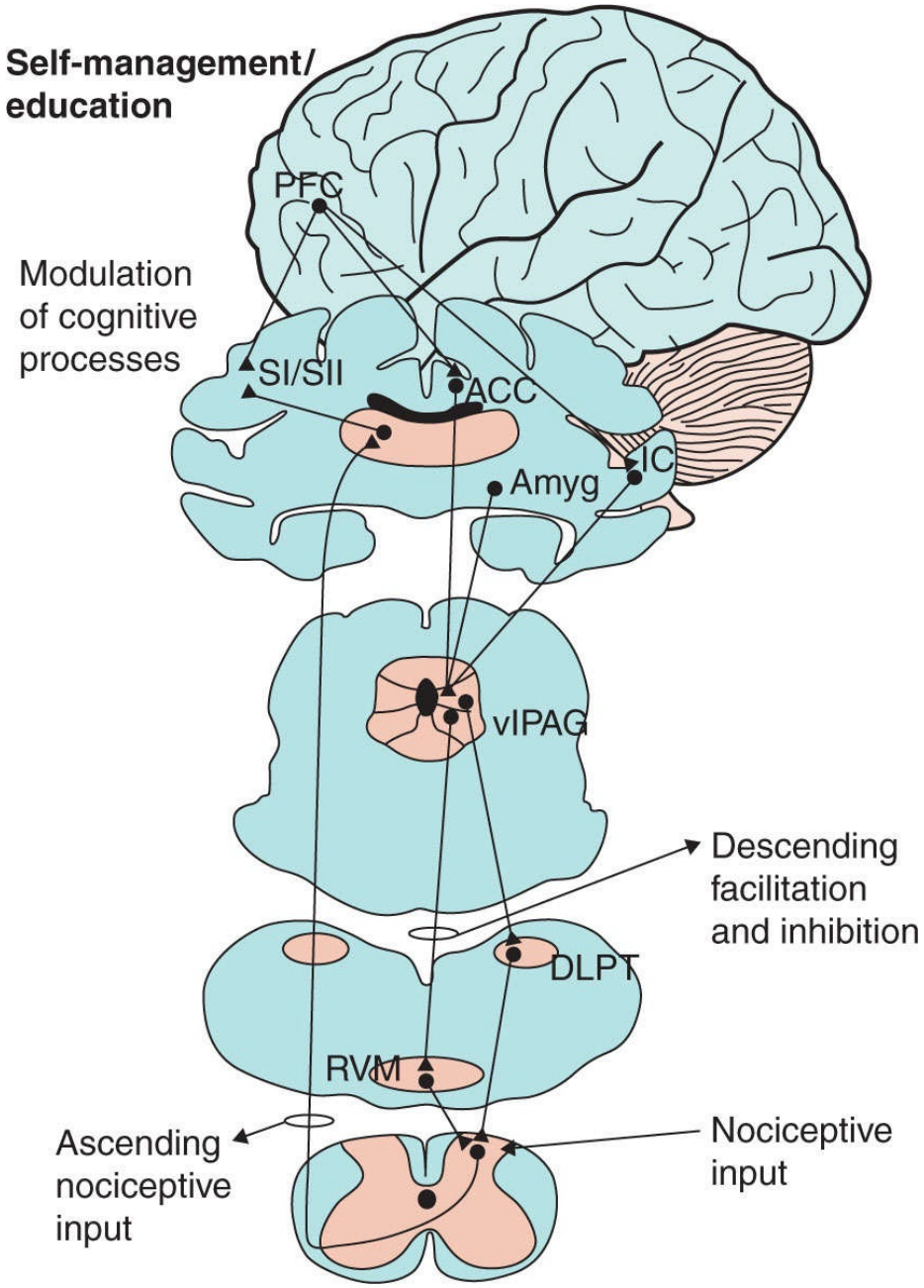

FIGURE 9-2 Schematic diagram indicating the potential underlying neurobiological mechanisms that could modulate nociceptive processing by education and self-management programs. Several pathways could be involved in the process, including the prefrontal cortex (PFC), which is involved in decision making and interpretation of input. The PFC sends modulatory input to other cortical areas involved in nociceptive processing, including the sensory cortices (SI/SII), as well as those areas involved in emotions (ACC, IC) and fear (amygdala; Amyg). These areas can then modulate brainstem activity by increasing inhibition through the periaqueductal gray–rostral ventromedial

medulla (PAG-RVM) pathway or by decreasing facilitation in this same pathway. Alterations in this facilitation and inhibition in the CNS would manifest as less activity of nociceptive neurons in the spinal cord, and this could decrease nociceptive input up the spinothalamic tract and other ascending nociceptive systems to ultimately decrease pain perception, in line with the Secondary modulation pathway presented in Figure 9.1.

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CONFLICTS OF INTERESTS

GLM received author royalties for books that are mentioned in this chapter: Explain Pain, Explain Pain Handbook: Protectometer, Painful Yarns—Metaphors and Stories to Help Understand the Biology of Pain all published by NOIgroup Publications, Adelaide, Australia.

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CHAPTER 10

Exercise-Induced Hypoalgesia: An Evidence-Based Review

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Participation in physical activity is important for overall health and wellness. Specific to pain, self-reported physical activity is associated with endogenous pain modulation (i.e., temporal summation [TS] and conditioned pain modulation [CPM]) in young and older adults [87,108]; adults who participate in higher levels of physical activity have more effective pain modulation. Similarly, prolonged physical inactivity or sedentary behavior can cause serious health detriments. A meta-analytic review concluded "prolonged sedentary time was independently associated with deleterious health outcomes regardless of physical activity" [14]. Therefore, an individual can be physically active and still experience negative health consequences if he or she has protracted sedentary time. Whether pain modulation improves with increased physical activity or decreased sedentary time has yet to be determined. This has important clinical implications because many individuals with chronic pain are physically inactive and have abnormal pain modulation.

Exercise is a subset of physical activity that is planned and structured with a focus on physical fitness [23]. Exercise is frequently prescribed by physical therapists and is an important component of rehabilitation, including the management of pain across the life span [86,139]. Individuals who regularly exercise report less pain over a 12-month time period and are less likely to develop chronic pain compared with those who are sedentary [78,79]. In a systematic review on the use of pedometers to promote physical activity, pain relief occurs with the increase in walking for individuals with musculoskeletal diseases [96]. Thus, increasing physical activity through exercise can help treat and possibly prevent chronic pain.

Exercise is a mainstay of physical therapy interventions. In conjunction with pain management, the majority of patients will be prescribed an exercise program to increase physical activity, increase strength, and restore normal

motion. There are numerous forms of exercise including stretching, strengthening, motor control, coordination, endurance, and aerobic. The purpose of this chapter is to review the evidence pertaining to exercise-induced changes in pain and the potential mechanisms responsible.

EXERCISE-INDUCED HYPOALGESIA IN HEALTHY SUBJECTS

A meta-analytic review examining pain perception (pain thresholds and pain intensity) following a single exercise session concluded exercise reduced experimental pain perception with mean effect sizes of moderate (aerobic) to large (isometric and dynamic resistance) in healthy adults [105]. Regardless of the type of exercise, pain relief following exercise is systemic. From a clinical perspective, exercise does not have to be performed by the painful body part to achieve a decrease in pain. Whether greater hypoalgesia occurs in the exercising limb compared with nonexercising body is inconclusive. Some studies show greater pain relief in the contracting muscle compared with distal body sites [76,146] whereas others have shown similar exercise-induced hypoalgesia (EIH) [67].

Aerobic exercise most consistently produces a hypoalgesic response when performed at moderate/high intensities and longer duration. When duration is the same, greater EIH occurs with higher-intensity aerobic exercise [107,146]. When the intensity is kept constant (75% VO_2 max), EIH occurs following 30 minutes, but not 10 minutes, of treadmill exercise [59]. Taken together, EIH following aerobic exercise is dependent on the intensity and duration of the exercise.

Both low- and high-intensity isometric exercise protocols produce hypoalgesia. Given the same duration (2 × 90 seconds), higher-intensity isometric contractions produce greater EIH than contractions performed at lower intensity (60% and 30% maximal voluntary contraction [MVC], respectively) [146]. Fatigue, which is demonstrated by a reduction in force-generating capacity of the muscle, is not required for EIH to occur. Following the performance of three brief MVCs, there was a decrease in pain perception although the force was similar across the three trials [8]. With lower-intensity (25% MVC) isometric contractions, longer duration is necessary to illicit pain relief [8]. Interestingly, this relation between intensity and duration may decline with age. Older adults had similar EIH following isometric contractions that varied in intensity and duration [86]. Most of the EIH research for healthy adults

has been conducted with younger individuals, which may impact the ability to translate the findings across the life span.

The inclusion of quantitative sensory testing (e.g., CPM and TS) has provided insight into the effect of exercise on central pain modulation. There is strong evidence that exercise across a multitude of doses decreases pain facilitation in young healthy adults. Both exhaustive (40% MVC held to exhaustion) and nonexhaustive (25% MVC × 3 minutes) isometric contractions decrease TS [72,106]. Specific to aerobic exercise, running on a treadmill to exhaustion, stationary cycling at a comfortable rate, and comfortable cycling followed by cycling to exhaustion decrease TS [152]. Furthermore, when exercise is painful the magnitude of EIH is greater than nonpainful exercise, suggesting that exercise may work through activation of descending inhibitory pathways (e.g., CPM) [38]. In young and older healthy adults, CPM predicts EIH; adults with greater CPM are more likely to report greater EIH [87]. Not all studies show this relation between CPM and EIH; mixed results have been shown with similar exercise doses [146,147]. Thus, exercise can decrease pain facilitation and is associated with pain inhibition in young healthy adults.

EIH IN SUBJECTS WITH PAIN

In people with chronic pain, there is greater variability in the pain response following acute exercise [105]. Additionally, less is known regarding the effect of acute exercise on central pain modulation. For people with rheumatoid arthritis, TS decreases following submaximal cycling [100]. In contrast, TS increases following a maximal treadmill test in people with fibromyalgia [152]. In people with low back pain, stationary cycling (5 minutes) or lumbar extension exercises (3 set of 15 reps) did not change TS [12]. Whether the equivocal results are due to the pain condition or exercise dose is not known. Minimal evidence is available regarding the influence of exercise on descending inhibitory pain pathways (e.g., CPM). In people with rheumatoid arthritis or chronic fatigue syndrome with comorbid fibromyalgia, the CPM response following a submaximal cycling test was inconclusive [100]. Overall, the effect of a single exercise session on central pain modulation for people in pain is mixed.

Distinguishing the difference between a single exercise session and exercise training on pain perception is important. Specifically, the pain response following exercise changes with time and may be dependent on the type of

exercise. In people with chronic neck pain, strengthening exercises may initially increase pain. With training, however, the acute increase in pain is no longer significant and this parallels the decrease in worst pain ratings (approximately 79%) [4]. In contrast, those individuals with chronic neck pain who participated in general fitness training (stationary cycling) had an acute but transient decrease in pain (<2 hours) with no changes in worst pain. Consequently, the pain response following a single exercise session does not reflect the potential benefits that can occur with exercise training.

The majority of systematic reviews conclude that participation in regular exercise decreases pain for a variety of pain conditions (Table 10-1). Although there is substantial evidence on the positive effect of exercise on pain, much of the research is of low quality (Table 10-1), making it difficult to determine specific dosing and overall effects. Another potential issue is the generalization of pain conditions (e.g., chronic musculoskeletal pain and painful shoulder). For example, many pain populations are considered chronic musculoskeletal pain but the response to exercise may not be uniform across these conditions, although the strength of these reviews is that they highlight the available evidence and general effectiveness of exercise in helping those with chronic pain.

Although the optimal dose and type of exercise is not known, increasing overall physical activity is beneficial. Five systematic reviews concluded that walking improved pain for individuals with chronic musculoskeletal pain [96,109], low back pain [56], knee osteoarthritis [93], and intermittent claudication [84]. Thus, with many pain conditions, participating in physical activity and/or incorporating specific exercises improves pain outcomes (Table 10-1). As the evidence evolves and improves in quality, specific recommendations may emerge. For instance, in the management of achilles tendinopathy, eccentric contractions are more effective than concentric exercise [120]. In summary, exercise prescription varies with each pain condition and increasing physical activity (e.g., walking) benefits the majority of people with chronic pain.

With many pain conditions, one exercise tends to be emphasized over others. One limitation of systematic reviews is that only the available evidence can be reviewed. For people with fibromyalgia, aerobic exercise was frequently recommended whereas strengthening exercises were underevaluated [19,20]. More recent reviews have concluded that moderate-/high-intensity resistance training is beneficial for people with fibromyalgia [21]. Similarly, with chronic low back pain, stabilization exercises tend to be emphasized in rehabilitation. One meta-analytic review concluded that stabilization exercises were equally effective as other active exercises [135] whereas another review recommended

stabilization exercises over cardiorespiratory exercise [125]. The first review did find that stabilization exercises were significantly more effective than other exercises, but the finding was clinically insignificant for minimal clinical important difference [135]. Therefore, differences in criteria and analysis within the systematic reviews may explain differing conclusions. Finally, there has been a surge of evidence showing the benefits of complementary exercises, including tai chi for arthritis [54,156], yoga and qigong for fibromyalgia [81,83], and Pilates for chronic low back pain [117]. There is a wide continuum of exercise prescription for pain management.

TABLE 10-1 **Evidence for Exercise-Induced Hypoalgesia**

Pain Condition	References	Title	Review Type	Pain Relief
Chronic musculoskeletal pain	[109]	Walking exercise for chronic musculoskeletal pain: systematic review and meta-analysis	Systematic review and meta-analysis	(+) Walking (fair quality); long-term effectiveness uncertain
Chronic musculoskeletal pain	[54]	The effectiveness of tai chi for chronic musculoskeletal pain conditions: a systematic review and meta-analysis	Systematic review and meta-analysis	(+) Tai chi for arthritis (low quality); unclear for other musculoskeletal pain
Musculoskeletal conditions	[6]	Effectiveness of aquatic exercise for musculoskeletal conditions: a meta-analysis	Systematic review and meta-analysis	(+) Aquatic exercise (moderate effects)
Fibromyalgia	[19]	Exercise for treating fibromyalgia syndrome	Cochrane review	(+) Supervised aerobic; strength and flexibility underevaluated
Fibromyalgia	[21]	Resistance exercise training for fibromyalgia	Cochrane review	(+) Moderate and moderate-/high-intensity resistance training (low quality); 8-wk aerobic exercise more effective than moderate-intensity resistance (low quality); 12-wk low-intensity resistance more effective than flexibility training (low quality)
Fibromyalgia	[13]	Aquatic exercise training for fibromyalgia	Cochrane review	(+) Supervised group aquatic training (low/moderate quality)
Fibromyalgia	[55]	Efficacy of different types of aerobic exercise in fibromyalgia syndrome: a systematic review and meta-analysis of randomized controlled trials	Systematic review and meta-analysis	(+) Slight-/moderate-intensity land-based or water-based exercise, 2–3/wk for 4 wk
Fibromyalgia	[81]	Efficacy and safety of meditative movement therapies in fibromyalgia syndrome: a systematic review and meta-analysis of randomized controlled trials	Systematic review and meta-analysis	(+) Yoga
Fibromyalgia	[83]	A systematic review and meta-analysis of qigong for the fibromyalgia syndrome	Systematic review and meta-analysis	(+) Qigong (low quality)
Mechanical neck disorders	[52]	Exercises for mechanical neck disorders	Cochrane review	Chronic neck pain: (+) cervico-scapulothoracic and upper-extremity strength training and (+) scapulothoracic and upper-extremity endurance training (moderate quality); (–) general fitness and (–) stretching alone (low quality) Chronic cervicogenic headache: (+) static–dynamic cervico-scapulothoracic strengthening/endurance (moderate quality) Acute radiculopathy: (+) cervical strength/strengthening/stabilization (low quality)
Chronic neck pain	[112]	Chronic neck pain and exercise interventions: frequency, intensity, time, and type principle	Systematic review	(+) Strengthening; effects improve with addition of stretching and aerobic exercise
Chronic nonspecific neck pain	[11]	Effect of therapeutic exercise on pain and disability in the management of chronic nonspecific neck pain: systematic review and meta-analysis of randomized trials	Systematic review and meta-analysis	(+)
Nonspecific neck pain (office workers)	[129]	Exercise therapy for office workers with nonspecific neck pain: a systematic review	Systematic review	(+) Muscle strengthening and endurance (strong evidence)

TABLE 10-1 **Evidence for Exercise-Induced Hypoalgesia (*continued*)**

Pain Condition	References	Title	Review Type	Pain Relief
Cervicobrachial pain	[122]	A systematic literature review on the effectiveness of noninvasive therapy for cervicobrachial pain	Systematic review and meta-analysis	Inconclusive
Acute low back pain or sciatica	[28]	Advice to rest in bed versus to stay active for acute low back pain and sciatica	Cochrane review	Little/no difference between advice to stay active, exercises, or physical therapy (low quality)
Acute and chronic low back pain	[56]	The effectiveness of walking as an intervention for low back pain: a systematic review	Systematic review	(+) Walking (low/moderate evidence)
Nonspecific chronic low back pain	[125]	Exercise interventions for the treatment of chronic low back pain: a systematic review and meta-analysis of randomized controlled trials	Systematic review and meta-analysis	(+) Strength/resistance; (+) coordination/stabilization; (–) cardiorespiratory and combined exercise
Nonspecific low back pain	[135]	An update of stabilization exercises for low back pain: a systematic review with meta-analysis	Systematic review and meta-analysis	Stabilization exercises equally effective as other active exercises (strong evidence)
Nonspecific chronic low back pain	[95]	Motor control exercise for persistent, nonspecific low back pain: a systematic review	Systematic review	(+) Motor control exercise as effective as other types of exercises
Nonspecific chronic low back pain	[117]	Effects of Pilates exercise programs in people with chronic low back pain: a systematic review	Systematic review	(+) Pilates
Low back pain	[24]	Exercises for prevention of recurrences of low back pain	Cochrane review	(+) Posttreatment exercise prevents back pain recurrences (moderate quality)
Lumbopelvic pain during pregnancy	[148]	Recommendations for physical therapists on the treatment of lumbopelvic pain during pregnancy: a systematic review	Systematic review	(+) Exercise (moderate quality)
Pelvic and back pain during pregnancy	[118]	Interventions for preventing and treating pelvic and back pain in pregnancy	Cochrane review	(+) Low back pain (low quality); adding belt to exercise improved pain (low quality); 8-to-20-wk exercise reduced risk of lumbopelvic pain (moderate quality); 16-to 20-wk exercise similar to usual care at preventing pelvic pain
Lumbar disc herniation with radiculopathy	[53]	Conservative management of lumbar disc herniation with associated radiculopathy: a systematic review	Systematic review	(+) Stabilization exercises (moderate evidence)
Lumbar disc surgery	[111]	Rehabilitation after lumbar disc surgery	Cochrane review	(+) Exercise 4-to-6-wk postsurgery; (+) high intensity more effective than low intensity (low/very low quality); (–) exercise immediately postsurgery
Lumbar spinal stenosis	[94]	Physical therapy interventions for degenerative lumbar spinal stenosis: a systematic review	Systematic review	(+) Exercise (low quality)
Lumbar spinal stenosis with neurogenic claudication	[3]	Nonoperative treatment for lumbar spinal stenosis with neurogenic claudication	Cochrane review	(+) Exercise improves leg pain (low quality)
Spondyloarthritis	[110]	Exercise therapy for spondyloarthritis: a systematic review	Systematic review	(+) Exercise (low evidence); supervised group better than unsupervised home exercise program
Osteoporotic vertebral fracture	[47]	Exercise for improving outcomes after osteoporotic vertebral fracture	Cochrane review	Inconsistent results (very low quality)
Osteoporotic/osteopenic postmenopausal women	[90]	Effects of exercise programs on quality of life in osteoporotic and osteopenic postmenopausal women: a systematic review and meta-analysis	Systematic review and meta-analysis	(+) Exercise; long-duration programs (>12 wk) better than short-duration; combined (strength, strength, and posture) better than strength alone

TABLE 10-1 **Evidence for Exercise-Induced Hypoalgesia (*continued*)**

Pain Condition	References	Title	Review Type	Pain Relief
Osteoarthritis (lower extremity)	[145]	Exercise for lower-limb osteoarthritis: systematic review incorporating trial sequential analysis and network meta-analysis	Systematic review and meta-analysis	(+) Strengthening; strengthening and flexibility; strengthening, flexibility, and aerobic; aquatic strengthening
Osteoarthritis (lower extremity)	[154]	Effect of therapeutic aquatic exercise on symptoms and function associated with lower-limb osteoarthritis: systematic review with meta-analysis	Systematic review and meta-analysis	(+)
Osteoarthritis (hip and/or knee)	[7]	Aquatic exercise for the treatment of knee and hip osteoarthritis	Cochrane review	(+) Aquatics in short term; no long-term effects documented
Osteoarthritis (knee)	[40]	Exercise for osteoarthritis of the knee	Cochrane review	(+) Land-based exercise; short-term benefits maintained 2–6 mo after cessation
Osteoarthritis (knee)	[142]	Efficacy of strengthening or aerobic exercise on pain relief in people with knee osteoarthritis: a systematic review and meta-analysis of randomized controlled trials	Systematic review and meta-analysis	(+) Exercise; non–weight-bearing strengthening better than weight-bearing strengthening or aerobic in short term
Osteoarthritis (knee)	[66]	Impact of exercise type and dose on pain and disability in knee osteoarthritis: a systematic review and meta-regression analysis of randomized controlled trials	Systematic review and meta-analysis	(+) Exercise; single-type exercise programs (aerobic, resistance, or performance) more effective than combination of different exercise types; supervised 3/wk; increasing supervised aerobic sessions increases effectiveness; quadriceps specific exercise increases effectiveness of resistance exercise
Osteoarthritis (knee)	[5]	Effect of home exercise program in patients with knee osteoarthritis: a systematic review and meta-analysis	Systematic review and meta-analysis	(+) Home exercise program
Osteoarthritis (knee)	[93]	Ottawa panel evidence-based clinical practice guidelines for aerobic walking programs in the management of osteoarthritis	Clinical practice guidelines	(+) Aerobic walking programs

Osteoarthritis (knee)	[156]	Effects of tai chi for patients with knee osteoarthritis: a systematic review	Systematic review	(+) Tai chi
Osteoarthritis (hip)	[41]	Exercise for osteoarthritis of the hip	Cochrane review	(+) Land-based exercise
Preoperative knee arthroplasty	[77]	Does preoperative physiotherapy improve outcomes in primary total knee arthroplasty? A systematic review	Systematic review	(–) Preoperative exercise (poor/moderate quality)
Preoperative knee or hip arthroplasty	[48]	Does exercise reduce pain and improve physical function before hip or knee replacement surgery? A systematic review and meta-analysis of randomized controlled trials	Systematic review and meta-analysis	(+) Preoperative exercise hip (medium effect); (–) preoperative exercise knee
Osteoarthritis (hand)	[70]	Systematic review of design and effects of splints and exercise programs in hand osteoarthritis	Systematic review	(+) Limited evidence
Osteoarthritis (hand)	[157]	Effects of rehabilitative interventions on pain, function, and physical impairments in people with hand osteoarthritis: a systematic review	Systematic review	(–)
Juvenile idiopathic arthritis	[141]	Exercise therapy in juvenile idiopathic arthritis	Cochrane review	(–)
Rheumatoid arthritis	[61]	Dynamic exercise programs (aerobic capacity and/or muscle strength training) in patients with rheumatoid arthritis	Cochrane review	(+) Combined aerobic and strengthening
Rheumatoid arthritis	[124]	Aerobic exercise is beneficial for people with rheumatoid arthritis	Systematic review	(+) Aerobic
Rheumatoid arthritis	[85]	Tai chi for rheumatoid arthritis: systematic review	Systematic review	(–) Tai chi (low quality)

TABLE 10-1 **Evidence for Exercise-Induced Hypoalgesia (*continued*)**

Pain Condition	References	Title	Review Type	Pain Relief
Painful shoulder	[97]	The effectiveness of therapeutic exercise for painful shoulder conditions: a meta-analysis	Systematic review and meta-analysis	(+)
Nonspecific shoulder pain	[149]	Effectiveness of soft tissue massage and exercise for the treatment of nonspecific shoulder pain: a systematic review with meta-analysis	Systematic review and meta-analysis	(+)
Adhesive capsulitis	[115]	Manual therapy and exercise for adhesive capsulitis (frozen shoulder)	Cochrane review	Combination of exercise and manual therapy less effective than glucocorticoid injection in short term
Adhesive capsulitis	[63]	The effectiveness of physiotherapeutic interventions in treatment of frozen shoulder/adhesive capsulitis: a systematic review	Systematic review	(+) Exercise strongly recommended for Stages 2 and 3 frozen shoulder
Rotator cuff tendinopathy	[92]	Therapeutic exercise for rotator cuff tendinopathy: a systematic review of contextual factors and prescription parameters	Systematic review	(+) Exercise with some level of resistance; exercise at home or in clinic similar; pain-producing or pain-avoidance exercise similar; three sets better than one or two sets
Shoulder impingement	[36]	Treatments for shoulder impingement syndrome: a PRISMA systematic review and network meta-analysis	Systematic review and meta-analysis	(+)
Shoulder impingement	[123]	Conservative treatment or surgery for shoulder impingement: systematic review and meta-analysis	Systematic review and meta-analysis	Active exercise similar to surgery (moderate evidence)
Upper limb fracture	[18]	Exercise reduces impairment and improves activity in people after some upper limb fractures: a systematic review	Systematic review	(+)
Patellofemoral pain syndrome	[150]	Exercise for treating patellofemoral pain syndrome	Cochrane review	(+) Exercise in short and long term (very low quality)
Patellofemoral pain syndrome	[25]	Effectiveness of exercise therapy in treatment of patients with patellofemoral pain syndrome: systematic review and meta-analysis	Systematic review and meta-analysis	(+) Short-term effects (≤12 wk); (–) long-term effects (≥26 wk)
Patellofemoral pain syndrome	[73]	Effects of physical therapist-guided quadriceps-strengthening exercises for the treatment of patellofemoral pain syndrome: a systematic review	Systematic review	(+) Quadriceps strengthening with/without other interventions
Achilles tendinopathy	[120]	Conservative management of midportion Achilles tendinopathy: a mixed methods study, integrating systematic review and clinical reasoning	Systematic review	(+) Eccentric (strong evidence); concentric less effective than eccentric (moderate evidence)
Lateral epicondylitis	[27]	Is eccentric exercise an effective treatment for lateral epicondylitis? A systematic review	Systematic review	(+) Eccentric
Delayed-onset muscle soreness	[58]	Stretching to prevent or reduce muscle soreness after exercise	Cochrane review	(–) Stretching before and/or after exercise
Intermittent claudication	[80]	Exercise for intermittent claudication	Cochrane review	(+)
Intermittent claudication	[39]	Supervised exercise therapy versus nonsupervised exercise therapy for intermittent claudication	Cochrane review	(+) Supervised more effective than nonsupervised
Intermittent claudication	[84]	Modes of exercise training for intermittent claudication	Cochrane review	(+) Supervised walking, cycling, strength training, and upper extremity ergometry
Cancer survivors	[101]	Exercise interventions on health-related quality of life for cancer survivors	Cochrane review	(+)
Cancer patients	[102]	Exercise interventions on health-related quality of life for people with cancer during active treatment	Cochrane review	(–)

TABLE 10-1 **Evidence for Exercise-Induced Hypoalgesia (*continued*)**

Pain Condition	References	Title	Review Type	Pain Relief
Breast cancer	[116]	Tai chi chuan exercise for patients with breast cancer: a systematic review and meta-analysis	Systematic review and meta-analysis	(–)
Shoulder pain in breast cancer	[143]	The efficacy of exercise therapy in reducing shoulder pain related to breast cancer: a systematic review	Systematic review	(+) Poor quality
Upper-extremity impairment after breast cancer surgery	[31]	Effectiveness of postoperative physical therapy for upper-limb impairments after breast cancer treatment: a systematic review	Systematic review	(+)
Shoulder dysfunction in head and neck cancer	[22]	Exercise interventions for shoulder dysfunction in patients treated for head and neck cancer	Cochrane review	(+) Progressive resistance training (limited evidence)
Headache and temporomandibular disorder	[43]	Does exercise therapy improve headache? A systematic review with meta-analysis	Systematic review and meta-analysis	(+) Tension-type headache and temporomandibular disorder
Dysmenorrhoea	[17]	Exercise for dysmenorrhoea	Cochrane review	(+) Limited evidence and poor quality
Chronic prostatitis/chronic pelvic pain	[26]	Therapeutic intervention for chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS): a systematic review and meta-analysis	Systematic review and meta-analysis	(+) Aerobic exercise
Postpolio syndrome	[74]	Treatment for postpolio syndrome	Cochrane review	(+) Muscle strengthening (very low quality)
Spinal cord injury chronic pain	[16]	Nonpharmacological interventions for chronic pain in people with spinal cord injury	Cochrane review	Insufficient evidence
Exercise-related groin pain	[1]	Conservative interventions for treating exercise-related musculotendinous, ligamentous, and osseous groin pain	Cochrane review	(+) Hip and abdominal strengthening (low quality)

Note: Selected systematic reviews summarizing the evidence for exercise-induced hypoalgesia for patient populations. Listed under "pain relief" are overall conclusions from the specific review regarding the effects of exercise on pain management including research quality and strength of the evidence.

When prescribing exercise, it is noteworthy that the benefits of exercise extend beyond pain relief. The American College of Sports Medicine recommends aerobic and strengthening exercises in the promotion of health and wellness. Furthermore, many people with chronic pain are deconditioned and would benefit from cardiovascular training. In contrast, resistance training is recommended as people age because with aging there is a reduction in muscle mass and function that negatively impacts function. Taken together, physical therapists may combine different forms of exercise to individualize a program to the person in pain.

Despite the overwhelming evidence on the pain-relieving aspects of exercise, some of the systematic reviews concluded that exercise is not beneficial. For example, systematic reviews on stretching for delayed-onset muscle soreness [58], exercise for acute low back pain [28] and juvenile idiopathic arthritis [141], and tai chi in rheumatoid arthritis [85] found no effect on pain. Similarly, the results are inconclusive on the effect of exercise on pain with osteoporotic vertebral fractures, mainly due to very low-quality evidence [47]. This does not mean, however, that exercise should not be prescribed because many of the systematic reviews reported therapeutic effects beyond pain relief (e.g., improvements in function, strength, and cardiovascular fitness).

In addition to human research, there is strong animal research that supports the pain-relieving aspects of exercise. Aerobic exercise in particular alleviates neuropathic pain induced by nerve injury or diabetes and chronic muscle pain induced by repeated acid injections [9,75,89,126,127,136]. In animals with neuropathic pain, treadmill running (16 m/min, 8% grade, high intensity) decreased the duration of pain sensitivity with significant reductions starting 3 weeks after exercise [136]. Like some of the human research there was a dose

effect; analgesic effects were similar if the animals exercised 3 d/wk or 5 d/wk, but did not occur at a lower intensity (10 m/min). Overall, there is substantial human and animal research supporting therapeutic exercise as a pain management tool.

Adherence

Many people discontinue exercise despite receiving benefits. Barriers to physical therapy treatment adherence are related to low levels of physical activity, low self-efficacy, depression, anxiety, poor social support, and increased pain during exercise [62]. In addition to patient attributes that influence adherence, the health care provider also influences exercise participation. Health care professionals with a more biomedical treatment approach to low back pain were more likely to recommend activity restriction than those with a biopsychosocial orientation [60]. Strategies to improve exercise adherence include supervision and self-management techniques [65]. Accordingly, both patient and practitioner attributes are important to address in the promotion of exercise adherence.

EXERCISE-INDUCED HYPERALGESIA

Pain with exercise is a barrier to exercise participation [34]; increases in pain occur in both human and animal studies following a single bout of exercise [29,82,133,137,152,158]. Importantly, pain during exercise does not prevent hypoalgesia from occurring following exercise cessation. Following an exhaustive isometric contraction, pressure pain ratings decreased for healthy adults despite severe (7/10) peak pain reports during exercise [87]. Furthermore, with exercise training, the majority of studies support the use of exercise for pain relief. Of the few systematic reviews that concluded exercise was not effective for pain relief, none of them reported pain exacerbation (Table 10-1).

The variability in the pain response (increase, decrease, and no change) occurs with several exercise protocols and occurs more frequently with chronic pain conditions [105]; women with fibromyalgia experience pain variability following isometric contractions that vary in both intensity and duration (Fig. 10-1) [10]. People with chronic pain may be susceptible to atypical pain responses with exercise in part because of abnormal pain modulation and low physical activity levels. For example, TS predicts sensitivity to physical activity (i.e., change in discomfort levels during 6-minute walk) in individuals with knee

osteoarthritis [155]. Furthermore, acute exercise can enhance pain facilitation in individuals with chronic pain [152], whereas exercise training has been found to attenuate pain facilitation [57]. Finally, physical activity levels are negatively associated with contraction-induced muscle pain for women with and without fibromyalgia [144]. Thus, there are a multitude of factors involved in the pain response following exercise, especially for individuals with chronic pain.

The underlying mechanisms of exercise-induced pain have been studied and extensively reviewed elsewhere (Sluka [131]) but will be summarized here. In humans, eccentric exercise (lengthening contractions) produces pain and muscle soreness to pressure for several days and has been termed delayed-onset muscle soreness [42,130]. Animal models have been developed to study the underlying mechanisms of eccentric exercise-induced pain [2,35,45]. Muscle nociceptors show increased sensitivity to mechanical stimulation of the muscle after eccentric exercise [140], and muscle damage is associated with increased pro-inflammatory cytokine release and infiltration of inflammatory cells in muscle [2,35,45]. Muscle nociceptors increase expression of the neuropeptide calcitonin gene-related peptide and of the ATP-receptor P2X3 [35]; blockade of TRPV1 channels (heat effect) or acid sensing ion channels (ASICs; decreased pH/lactic acid effect) prevents the eccentric exercise-induced mechanical hypersensitivity [45]. Together, the data suggest that eccentric exercise results in release of inflammatory mediators that subsequently activate nociceptors resulting in enhanced sensitivity to mechanical stimuli and pain.

Interestingly, a prior eccentric exercise task enhances the response to a subsequent injection of the inflammatory mediator prostaglandin E-2 (PGE-2) [2]. Reduction of the intracellular messenger protein kinase Cε (PKCε) or the inflammatory cytokines receptor to interleukin-6 in nociceptors prevents the enhanced effect of eccentric exercise-induced hyperalgesia to PGE-2. This suggests that eccentric exercise results in a sensitization of nociceptors that involves IL-6 receptors and activation of PKCε so that a subsequent noxious stimulus results in an enhanced pain response.

Similarly, a nondamaging exercise task in combination with a subthreshold muscle insult produces mechanical hypersensitivity [51,131,133,158] in a sex-dependent manner with females showing greater and longer-lasting hyperalgesia [51,134]. In these animal models, changes indicative of enhanced neuron excitability are observed in the central nervous system with increases in activation of cells (c-fos and enhanced p-NR1) in the caudal raphe nuclei of the medulla—nucleus raphe magnus, nucleus raphe pallidus, and nucleus raphe obscurus [132,134]. There are also changes peripherally with decreases in pH and activation of ASIC3 [50]. Further, fatiguing exercise increases the number of

macrophages in muscle and removal of macrophages prevents exercise-induced hyperalgesia [50]. These data suggest increased activation and sensitization of central neurons, release of fatigue metabolites and activation of their receptors, and alterations in immune system function locally in muscle underlie the exercise-induced pain.

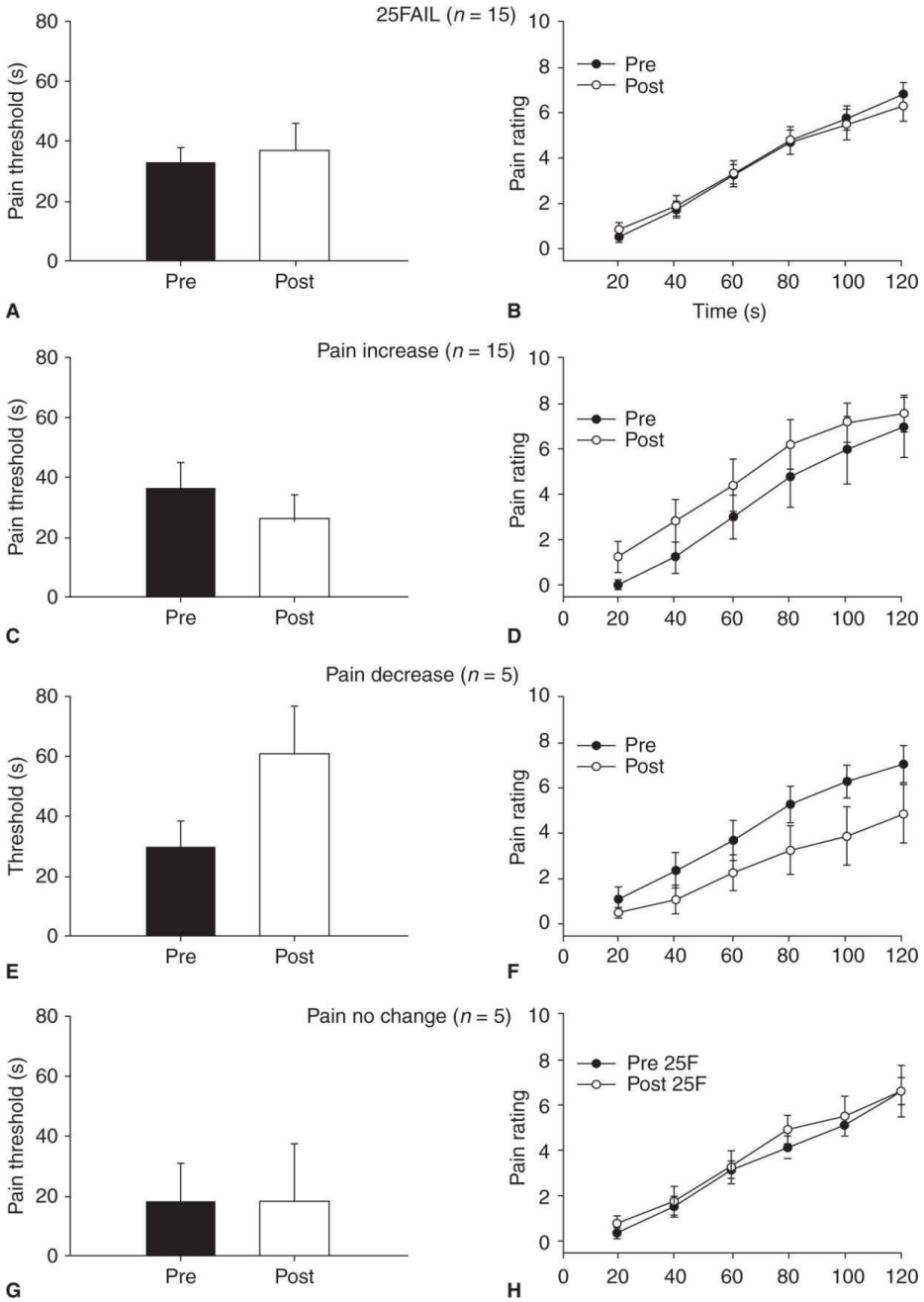

FIGURE 10-1 Fifteen women with fibromyalgia completed a submaximal (25% maximal voluntary contraction) isometric contraction of the left elbow flexors sustained held until task failure (25FAIL). There was no significant difference in

pain threshold **(A)** or pain ratings **(B)** after the sustained contraction. Based on the pain response, participants were divided into three groups (pain increase **[C, D]**, pain decrease **[E, F]**, and no change in pain **[G, H]**). There was a significant interaction between trial and pain response for both pain threshold and pain ratings demonstrating significant variability in the pain response following exercise in women with fibromyalgia. (From Bement et al. [10].)

Pain with exercise should not be a barrier to exercise participation. Physical therapists have the necessary expertise to provide appropriate exercise prescription in parallel with supplemental pain management and patient education. For example, pain with movement is decreased with transcutaneous electrical nerve stimulations in people with fibromyalgia [29]. Education should include that pain relief occurs gradually, slight increases in pain may occur initially, and slight increases do not indicate tissue injury but rather the body is adapting to exercise [91].

Mechanisms of EIH

The biopsychosocial model incorporates biological, psychological, and sociocultural variables in how someone reports pain (see Chapter 1). Regular exercise can impact each of these variables. In relation to biological variables, exercise can help modify the disease activity and improve overall physical conditioning. Psychological variables, such as pain catastrophizing, are related to the magnitude of EIH [106] and have been found to improve with exercise [153]. Sociocultural factors may be addressed by performing exercises in a support group or with family members, which also improves adherence [30]. Therapists need to take into account the entire biopsychosocial model when prescribing exercise to enhance pain relief.

Quantitative sensory testing has provided additional insight into how exercise impacts central pain modulation. The strongest evidence is in healthy adults showing that exhaustive and nonexhaustive exercise decreases pain facilitation (i.e., TS). In regard to pain inhibition, CPM is associated with the magnitude of EIH and physical activity levels. Less is known regarding the influence of exercise on central pain modulation in patient populations. Furthermore, research identifying whether abnormal endogenous pain modulation often seen in chronic pain populations alters pain responses following exercise is ongoing.

The most studied EIH mechanism is activation of the opioid system (see Chapter 2). Evidence from both humans and animals has identified the

contribution of the opioid system in EIH. In animals without tissue injury, blockade of opioid receptors systemically reduces analgesia produced by chronic running wheel activity and by strength training [89,99]. In contrast, administration of an opioid antagonist did not affect hypoalgesia following a submaximal isometric exercise in healthy humans [71]. This study highlights that there are multiple mechanisms contributing to pain relief following exercise and activation of the opioid system is not always involved.

Less is known regarding activation of the opioid system for people with chronic pain. A systematic review on the effects of exercise on pain-relieving peptides (e.g., endogenous opioids, serotonin, and norepinephrine) in the plasma or cerebral spinal fluid in people with musculoskeletal pain resulted in one low-quality article [44]. In animal models of pain, several studies demonstrate that opioid receptors are involved in the analgesia produced by regular exercise. Blockade of opioid receptors, systemically and in the brainstem, prevents the analgesia produced by regular aerobic exercise in neuropathic pain, chronic muscle pain, and acetic acid–induced pain [9,98,99,126,136]. Furthermore, there is an increased release of endogenous opioids in the periaqueductual gray (PAG) and rostral ventral medulla (RVM) in response to aerobic exercise in animals with neuropathic pain [136]. On the other hand, blockade of peripheral opioid receptors has no effect on the exercise-induced analgesia in animals with neuropathic pain [136]. Recent studies, however, show peripheral expression of opioid peptides in muscle [33], suggesting that exercise may also produce its effects by activation of peripheral opioid receptors. In women with chronic neck pain, exercise training increases β-endorphins in the trapezius muscle and decreased pain reports [69]. The change in pain intensity, however, was related to changes in cortisol and glutamate, but not β-endorphins, in the trapezius muscle [69].

In combination with activation of the opioid system, other central mechanisms contribute to EIH. For example, serotonin is a major neurotransmitter found in endogenous inhibitory pathways including the PAG, RVM, and spinal cord and plays a significant role in analgesia. In healthy humans, prolonged gum chewing decreases nociceptive reflexes and increases serotonin, suggesting that exercise may decrease nociception through serotonergic descending inhibitory pathways [68,103]. In animals without tissue injury, aerobic exercise-induced analgesia is prevented by prior depletion of serotonin with p-chlorophenylalanine [99]. Specific to the hippocampus, regular running wheel exercise increases opioid receptor expression in the hippocampus [32] as well as learning, memory, and neurogenesis [15,128]. Voluntary exercise also reduces depressive behaviors in mice with concomitant changes in brain-

derived neurotrophic factor in the hippocampus [37]. Cognitive dysfunction and depression are comorbid symptoms found in people with chronic pain conditions [49,151]. Additionally, changes in autonomic function occur in chronic muscle pain in people and in animals [121,137] and include decreased baroreflex sensitivity, increased blood pressure variability, and decreased heart rate variability. These autonomic changes induced by chronic muscle pain are prevented by either 5 days or 8 weeks of regular physical activity. Thus, additional benefits of regular exercise in people with chronic pain could be to improve learning, reduce depression, and reverse autonomic dysfunction.

Regular exercise can also prevent the development of chronic pain, potentially through changes in central neurons. Mice that participated in regular physical activity did not develop an increase in mechanical sensitivity that the sedentary mice did following intramuscular acidic injections (Fig. 10-2) [133]. Furthermore, the increase in phosphorylation of the NR1 subunit of the NMDA receptor, a measure of central excitability, which typically occurs following the muscle insult, was prevented in the animals that regularly exercised (Fig. 10-2). Thus, central mechanisms are likely involved for the effects that exercise has in the decrease and potentially prevention of chronic pain.

Evidence also supports the role of peripheral mechanisms through reduced nociceptor activity or enhanced endogenous inhibitory neuromodulators. In animals with diabetic neuropathy, there is enhanced calcium current density for both low- (LVA) and high-voltage calcium currents (HVA) in dorsal root ganglia neurons [126], which is indicative of enhanced nociceptor activity. Treadmill running reduces the enhanced current densities of HVA and LVA calcium channels, suggesting reductions in nociceptor activity. Regular exercise may reduce pain hypersensitivity by normalization of enhanced ion channel activity of nociceptors. In addition to ion channels, pain is influenced by neurotrophic factors, particularly members of the nerve-growth factor family of neurotrophins. After 3 weeks of exercise in mice with noninflammatory muscle pain, there is increased expression of NT-3 mRNA and protein in the muscle tissue [127] in the same time period when significant reductions in pain behaviors are observed. Neurotrophin-3 is analgesic when injected or overexpressed in muscle [46], and thus these data suggest that exercise could increase NT-3 in muscle to reduce nociceptive activity and produce analgesia.

Lastly, regular physical activity can alter the state of the immune system. Regular physical activity in healthy individuals alters cytokine profiles with decreases in expression of pro-inflammatory cytokines, such as TNF-α and IL-6, and increases in IL-10, an anti-inflammatory cytokine [64,119]. Similarly, people with fibromyalgia show higher circulating levels of inflammatory

cytokines (IL-8, IFN-γ) and enhanced evoked release of inflammatory cytokines (TNF-α, IL-1β, IL-6) from monocytes [113,114] when compared with healthy controls. Regular exercise reduces circulating and evoked release of inflammatory cytokines, and increased evoked release of IL-10 from monocytes in fibromyalgia subjects [113]. In animals, long-term physical activity (8 weeks) increases the percentage of muscle macrophages that express CD206, indicating an increase regulatory M2 macrophage phenotype [88]. Regulatory macrophages secrete anti-inflammatory cytokines and their main function is to dampen the immune response upon removal of infectious microbes, limit inflammation, and promote tissue repair and restoration of homeostasis [104]. Regular physical activity prevents the development of chronic muscle pain that is prevented by local blockade of IL-10 in muscle and mimicked by local administration of IL-10 [88]. Taken together with the previous studies, peripheral and central neural mechanisms, as well as alterations in the immune system, are likely responsible for EIH.

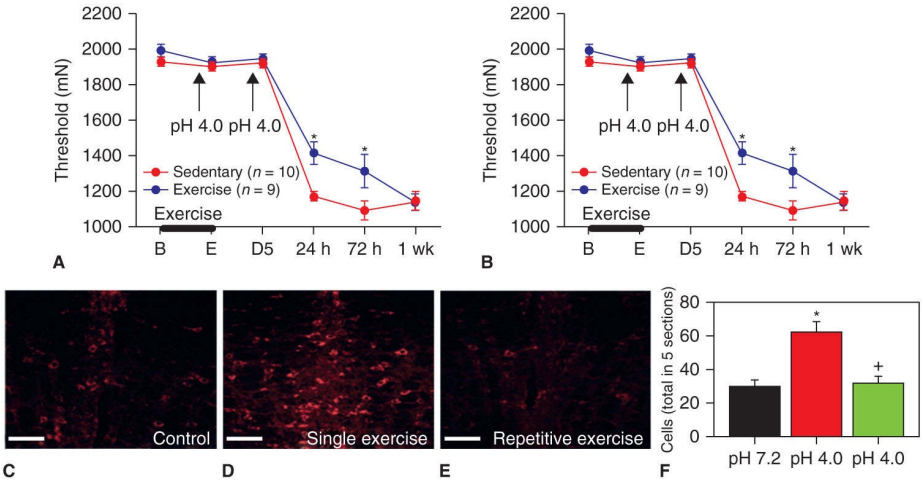

FIGURE 10-2 This figure shows data from mice that performed 8 weeks of regular physical activity prior to induction of a chronic muscle pain model and were compared with sedentary mice. Physically active mice were given free access to running wheels in their cages prior to induction of the chronic pain model with two intramuscular injections of pH 4.0 saline. Sedentary mice develop an increased sensitivity to mechanical stimuli applied to the muscle (**A**, decreased withdrawal threshold) and to the paw (**B**, increased response to repeated stimuli) for weeks after injection. Animals that performed 8 weeks of physical activity did not develop the hyperalgesia of the muscle or paw. The effects of exercise lasted for approximately 1 week after stopping the activity at the time of induction. To measure activity of neurons the phosphorylation of the NR1 subunit of the NMDA receptor was stained in the brainstem and rostral

ventromedial medulla (RVM). In response to two injections of pH 4.0 saline in sedentary mice there is a significant increase in the number of neurons stained for pNR1 **(D, F)**, when compared with sedentary mice injected with pH 7.2 as a control **(C, F)**. Eight weeks of running wheel activity prevented the increase in pNR1 that normally occurs in animals injected with pH 4.0 saline **(E, F)**. Bar, 50 mM, $*P < 0.05$. (Figures modified from Sluka et al. [133].)

SUMMARY

Evidence supports the use of therapeutic exercise in relieving pain for the majority of pain conditions. Research continues to evolve to identify the optimal dose and type. This is likely related to the pain condition and patient characteristics (e.g., biopsychosocial model). Patients should be instructed on the importance of increasing physical activity for pain benefits and overall health and wellness. Education should occur in parallel with therapeutic exercise and include the potential for an increase in pain with the initiation of exercise. In summary, exercise can reduce pain and disability, improve function, prevent the recurrence of pain, and prevent the development of chronic pain.

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CHAPTER 11

Transcutaneous Electrical Nerve Stimulation and Interferential Therapy

Kathleen A. Sluka and Deirdre M. Walsh

In the field of electrotherapy, the term transcutaneous electrical nerve stimulation (TENS) can be used to describe a range of electrical currents including neuromuscular electrical stimulation and interferential therapy (IFT). However, for the purposes of this text, TENS will be used to refer to only those devices that are used to apply low-voltage electrical currents to the skin primarily for the purposes of pain relief (Fig. 11-1). TENS is a safe, noninvasive treatment with relatively few contraindications that can be either self-administered or therapist-administered. Although early prototypes of TENS units were available from the late 1800s [117], a theoretical foundation for electroanalgesia did not emerge until Melzack and Wall's [67] pain gate theory was published in 1965. After the theory was published, clinical studies began reporting the success of *percutaneous* electrical stimulation for pain relief [116]. At that time, Shealy [95] began using an early TENS model as a screening device for his chronic pain patients who were being considered for dorsal column stimulation (DCS). Shealy discovered that some patients responded better to TENS than to DCS; subsequently, *TENS* emerged as a viable modality in the field of pain management. Since the 1970s, advances in technology have produced a range of electrodes and TENS units for clinicians to choose from.

IFT involves the application of two medium-frequency currents (i.e., in the range of 2000–4000 Hz) to the skin in order to produce an amplitude-modulated low-frequency (known as the amplitude modulated or beat frequency) effect within the tissues [74]. With the development of small portable devices, IFT can be either self-administered or therapist-administered (Fig. 11-2). The basic concept behind IFT is that skin impedance (resistance) is inversely proportional to the frequency of an applied current; therefore, there is less skin resistance to a frequency of 2000 Hz than a frequency of 200 Hz. It has been claimed that IFT can be used to treat deeper tissues because a lower pulse amplitude is required to

overcome the associated skin resistance. The two medium-frequency currents "interfere" within the tissues and produce a beat frequency, which is the difference between the values of the two applied medium frequencies. For example, if 4000 and 4150 Hz medium-frequency currents are applied to the skin, the resultant beat frequency within the tissues is 150 Hz (see Fig. 11-3). However, the scientific evidence behind the principle of IFT producing a low-frequency current within the tissues with a greater depth of penetration is seriously lacking. IFT has been used clinically since the 1950s but despite its popularity in physical therapy departments [31,76], limited data are available on its mechanisms of action and clinical efficacy [72].

FIGURE 11-1 Select TENS unit (Empi, United States).

FIGURE 11-2 Flexistim interferential TENS unit (TensCare, United Kingdom).

The objective of this chapter is to provide an overview of the pertinent research relating to the theory and clinical application of TENS and IFT. The majority of basic science and clinical literature focuses on TENS, both low and high frequency. However, there is literature emerging that supports the use of IFT for pain relief.

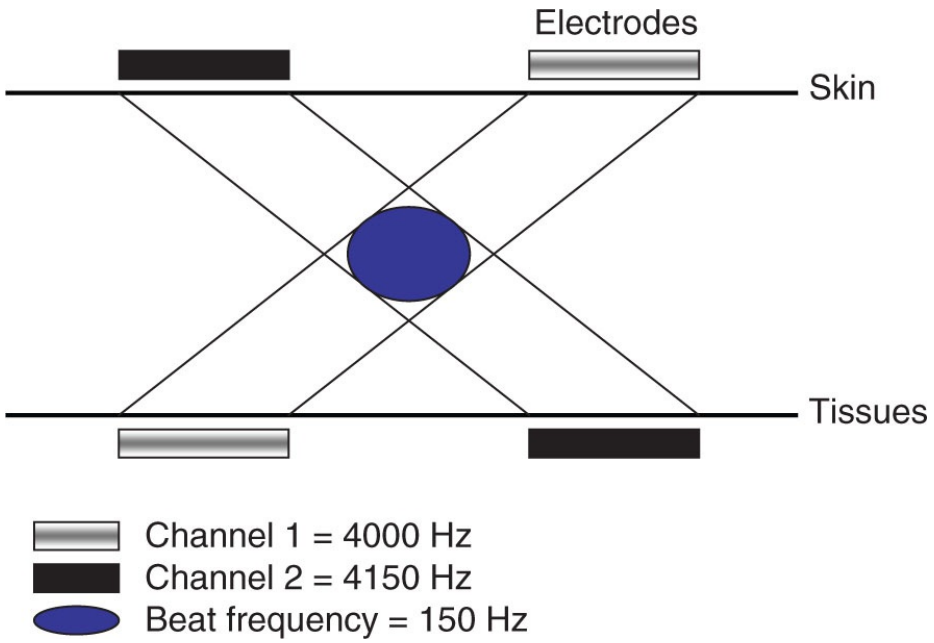

FIGURE 11-3 Principle of IFT: two medium-frequency currents applied to the skin to produce a low beat frequency within the tissues.

TENS AND IFT PARAMETERS

A typical TENS unit allows the parameters of pulse duration, frequency, pulse amplitude, and type of output (constant, burst, modulated) to be manipulated. Each of these parameters is briefly explained below:

Pulse duration is the length of each pulse (usually in μs or ms).
Frequency is the number of pulses delivered per second (usually in Hz).
Pulse amplitude refers to the strength of the output and is measured in mA or V depending on whether the device produces a constant current or constant voltage.
Type of output describes the pattern in which the pulses are delivered (see Fig. 11-4). A constant output produces pulses in a constant pattern over time. A burst output produces trains (or bursts) of pulses delivered at a low frequency while the internal frequency of the train is high. A modulated output means that the pulses are delivered in a pattern whereby one or several of the parameters are varied in a cyclical fashion (e.g., amplitude).

The most common modes (types) of TENS used in clinical practice are described as conventional or high-frequency TENS (>50 Hz) and acupuncture-

like or low-frequency TENS (1–10 Hz). Original TENS units used a carbon rubber and gel application, whereas most units today come with a supply of self-adhesive electrodes. Electrodes are typically placed at the site of injury or pain, proximal to the injury over a nerve supplying the affected area, or spinally at the appropriate segmental level.

In an IFT unit, the parameters that can be manipulated are beat frequency, sweep frequency, and pulse amplitude. The *beat frequency* is selected by manipulating the frequency of the two medium-frequency currents and ranges between 1 Hz and 150 Hz. For example, to produce a beat frequency of 100 Hz, one channel is set at 4000 Hz and the second is set at 4100 Hz. IFT can be applied using two or four electrodes with the same choice of electrode placement to that of TENS described above. In a four-electrode arrangement, a low-frequency effect is believed to be produced in the tissues as illustrated in Fig. 11-3. In a two-electrode arrangement, it is suggested that the medium-frequency currents mix within the unit and therefore a low-frequency "premodulated" current is delivered to the skin. Ozcan et al. [74] compared sensory, motor, and pain thresholds using premodulated IFT and "true" IFT in a group of healthy adults. They also compared crossed currents and parallel currents for each type of IFT. Their study concluded that "true" IFT had no measurable advantage over premodulated IFT in terms of depth efficiency (as assessed by thresholds), torque production, or comfort.

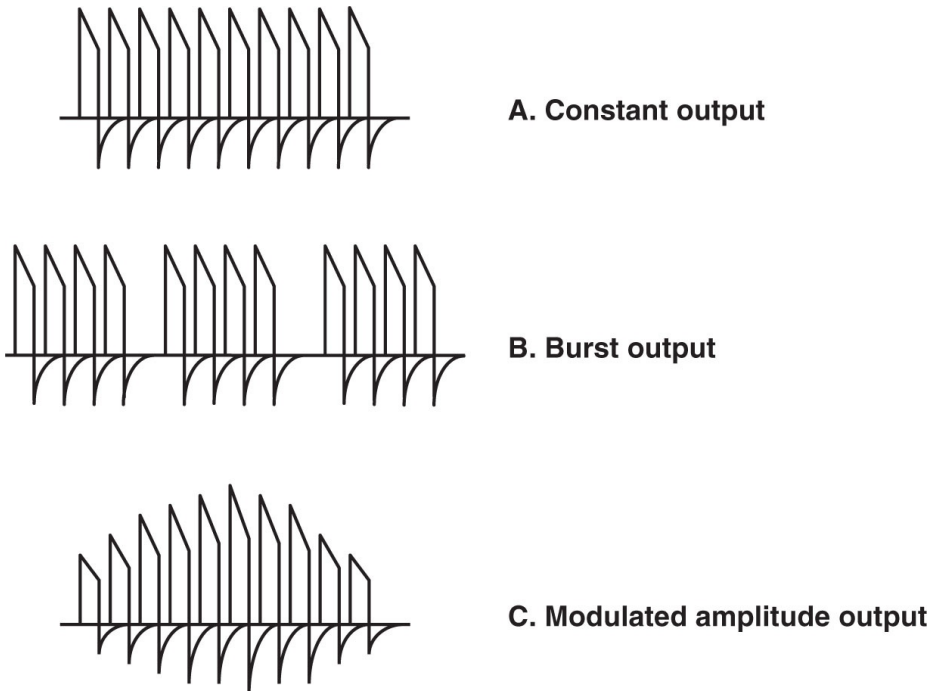

FIGURE 11-4 Types of TENS output.

Manipulation of the *sweep frequency* allows the therapist to move the beat frequency through a selected range (e.g., 100–120 Hz) during the treatment time. The pattern in which the beat frequency changes from highest to lowest levels can also be altered. For example, typical sweep patterns involve increasing the frequency over a 6-second time interval and then decreasing it over a 6-second interval (written as 6^6).

MECHANISMS OF TENS ANALGESIA

Two theories are commonly utilized to support the use of TENS. The gate control theory of pain is most commonly utilized to explain the inhibition of pain by TENS. According to the gate control theory of pain, stimulation of large-diameter afferents by TENS inhibits nociceptive fiber-evoked responses in the dorsal horn. There is now much more detailed data on mechanisms of actions of TENS that include anatomical pathways, neurotransmitters and their receptors, and the types of neurons involved in the inhibition. Release of endogenous opioids has been utilized to explain the actions of TENS, particularly low-frequency stimulation. Recent data support this theory for low-frequency TENS as well as for high-frequency TENS stimulation [51,104].

Early studies on mechanisms of action of TENS were performed in normal, uninjured animals. These studies provided valuable information regarding potential mechanisms of action of TENS. More recent studies have translated and extended these data by examining mechanisms of action of TENS in animal models of pain. The studies in animal models of pain have revealed pharmacological and anatomical pathways that mediate the reduction in pain produced by TENS [114]. The current data suggest that different frequencies of TENS produce analgesia through actions on different neurotransmitters and receptors (Table 11-1).

TABLE 11-1 **Summary of Basic Science Mechanisms for Low- and High-Frequency TENS**

	Low-Frequency TENS	High-Frequency TENS
Reduces primary hyperalgesia	+	+
Reduces secondary hyperalgesia	+	+
Reduces central sensitization	+	+
Activates PAG	+	+
Activates RVM	+	+
Activates spinal inhibitory mechanisms	+	+
Activates peripheral inhibitory mechanisms	+	+
Uses opioids	+ μ (cortex, RVM, SC, P)	+ δ (RVM, SC)
Uses serotonin	+ 5-HT_2, 5-HT_3 (SC)	– (SC)
Uses noradrenaline centrally	– (SC)	– (SC)
Uses α-2a adrenergic receptors	+ (P, not SC, not supraspinal)	+ (P, not SC, not supraspinal)
Uses GABA	+ (SC)	+ (SC)
Uses acetylcholine (activates muscarinic receptors)	+ M1, M3 (SC, not M2)	+ M1, M3 (SC, not M2)
Reduces glutamate release	–	+ (SC)
Reduces substance P release/ content	NT	+ (SC, P)
Reduces pro-inflammatory cytokines and PGE2	NT	+ (SC)
Reduces phosphorylation of ERK	NT	+(SC)
Activates autonomic nervous system	+ (P)	+ (P)

Abbreviations: PAG, periaqueductal gray; RVM, rostral ventromedial medulla; SC, spinal cord; P, periphery; NT, not tested.

Afferent Fibers Activated by TENS

Recordings from the median nerve in human subjects indicate that high-frequency (100 Hz), sensory intensity (3 × sensory threshold) stimulation activates only large-diameter Aβ fibers. Similarly, low-frequency (4 Hz) TENS, at a maximal tolerable intensity, only activates Aβ afferent fibers, whereas Aδ activation only occurs at intensities above maximal tolerable intensity [61]. Similarly, in animals, high- or low-frequency TENS at sensory intensity, or motor threshold, activates only large-diameter Aβ afferent fibers. Increasing the intensity to two times motor threshold recruits Aδ fibers with both low- and high-frequency TENS [82].

It is generally assumed that TENS reduces pain and hyperalgesia through

activation of cutaneous afferent fibers because patients “perceive the stimulus in the skin.” However, one animal study provides contradictory evidence to this assertion. Specifically, utilizing animals with knee joint inflammation, local anesthetic was applied to the skin under the electrodes or into the knee joint prior to TENS (either low- or high-frequency TENS at sensory intensities). TENS was equally effective, compared with placebo anesthetic, in animals where cutaneous afferents were anesthetized with local anesthetic; however, it was ineffective when knee joint afferents were anesthetized with lidocaine [82] supporting a role for deep tissue afferents in the pain relief produced by TENS. Thus, it can be concluded that TENS must be applied at sufficient intensities to activate large-diameter deep tissue afferent fibers to produce significant pain relief.

Neuronal Pathways Activated by TENS

Research over several years has discovered that TENS produces its analgesic effects through activation of pathways within the peripheral and central nervous system. As stated above, large-diameter afferent fibers are activated by TENS. This input is sent through the central nervous system to activate the descending inhibitory systems to reduce hyperalgesia. Specifically, blockade of activity in the periaqueductal gray (PAG), rostral ventromedial medulla (RVM), and spinal cord inhibits the analgesic effects of TENS [27,51,104] (for review of pain inhibition pathways see Chapter 3). Further, receptors at the site of injury also play a role in the analgesia produced by TENS [54,89]. Thus, TENS activates a complex neuronal network to result in a reduction in pain. Details of the pathways, neurotransmitters, and receptors involved in the analgesia by low- and high-frequency TENS will be presented below.

Effects of TENS in Animal Models of Pain

In animals without tissue injury, the responses to noxious thermal stimuli are increased after treatment with either high- or low-frequency TENS [121,122]. In parallel, dorsal horn neuron activity is reduced [33,34,57,98,99] by both low- and high-frequency TENS in animals without tissue injury. These data show that increasing frequency, pulse amplitude, or pulse duration results in a greater reduction in dorsal horn neuron activity, and further reduces the response to peripherally applied noxious stimuli [34].

Both low- and high-frequency TENS reduce hyperalgesia in a variety of animal models including those with tissue injury induced by inflammation of

skin, joint, or muscle, local incision to mimic postoperative pain, and nerve injury mimicking neuropathic pain [2,17–19,30,36,85,102,115]. Both primary and/or secondary hyperalgesia, to heat and mechanical stimuli, are reversed by both low-frequency (4 Hz) and high-frequency (100 Hz) TENS [2,17–19,30,36,85,102,115]. In a chronic model of muscle inflammation, hyperalgesia spreads to the contralateral hind limb [80]. In this case, application of TENS to the inflamed or the contralateral noninflamed muscle equally reduces the secondary hyperalgesia suggesting widespread effects of TENS. Further, sensitization of dorsal horn neurons to both noxious and innocuous stimuli that occur after peripheral inflammation is also reduced by either high- or low-frequency TENS [63]. In animal models of neuropathic pain, either high- or low-frequency TENS reduces hyperalgesia and sensitization of spinal neurons that normally occurs in these models [19,58,71,111]. Thus, TENS is analgesic in normal animals, reduces primary and secondary hyperalgesia in animals with tissue injury, and reduces central sensitization produced by tissue injury.

Analgesic Mechanisms of TENS

High-Frequency TENS

In animals that were spinalized to remove descending inhibitory pathways, inhibition of the tail flick by high-frequency TENS still occurs but is reduced by about 50% [122]. Thus, these studies suggest that both segmental and descending inhibition are involved in the analgesia produced by high-frequency TENS. Later studies prevented the analgesic effects of high-frequency TENS by blockade of δ-opioid receptors in the RVM, or blockade of synaptic transmission in the PAG, further supporting a role for supraspinal pathways in TENS analgesia [27,51].

Opioid peptides mediate the effects of high-frequency TENS. High-frequency TENS increases the concentration of β-endorphins in the bloodstream and cerebrospinal fluid, and increases methionine-enkephalin in the cerebrospinal fluid, in human subjects [38,90]. In animals with knee joint inflammation, blockade of δ-opioid receptors in the spinal cord or the RVM reverses the antihyperalgesia produced by high-frequency TENS [51,104]. Repeated daily application of high-frequency, motor intensity TENS produces tolerance (reduced effectiveness) to the antihyperalgesic effects of TENS using spinal δ-opioid receptors [15]. These opioid-mediated effects of high-frequency TENS have been confirmed in human subjects with chronic pain; high doses of

naloxone block the effects of high-frequency TENS [60]. Thus, high-frequency TENS activates classical inhibitory pathways in the central nervous system and uses δ-opioid receptors to produce the analgesia.

High-frequency TENS also enhances release of the inhibitory neurotransmitter GABA in the spinal cord dorsal horn and the TENS antihyperalgesia is reduced by blockade of $GABA_A$ receptors in the spinal cord [64]. Muscarinic receptors are also commonly implicated in analgesia at the level of the spinal cord, particularly with respect to opioid analgesia mechanisms. Indeed, the antihyperalgesia produced by high-frequency TENS is reduced by blockade of muscarinic receptors (M1, M3) in the spinal cord [81]. However, blockade of serotonin or noradrenergic receptors in the spinal cord has no effect on the reversal of hyperalgesia produced by high-frequency TENS [79]. Thus, a complicated neural circuitry is activated in response to high-frequency TENS that utilizes descending opioid inhibitory pathways that include the PAG, RVM, and spinal cord to reduce excitability of dorsal horn neurons through decreasing release of glutamate, increasing release of GABA, endogenous opioids, and acetylcholine to result in reduction of nociception and consequently pain.

High-frequency TENS reduces enhanced changes in excitatory neurotransmitters and modulators in the central nervous system. The enhanced release and expression of excitatory neurotransmitters glutamate and substance P in the spinal cord dorsal horn in animals with tissue injury are reduced by high-frequency TENS [18,86,108]. The reduction in glutamate is prevented by blockade of δ-opioid receptors linking the effects of TENS on excitatory neurotransmitter release to activation of inhibitory pathways. Pro-inflammatory cytokines are also enhanced in the spinal cord after tissue injury, and these increases are attenuated by high-frequency TENS [18]. Mixed frequencies of TENS (2 and 100 Hz) are also effective and reduce spinal release of the inflammatory mediator prostraglandin-E2, expression of the cyclooxygenase 2 enzyme involved in the production of prostaglandin-E2, and phosphorylation of the extracellular signal-related kinase, which is a key intracellular signalling protein involved in nociceptive transmission [30]. Thus, TENS not only activates inhibitory pathways, it also reduces release of excitatory neurotransmitters, cytokines, and their production, and enhances intracellular signalling.

High-frequency TENS also has effects in the peripheral nervous system. The primary afferent neuropeptide, substance P, which is normally increased in injured animals, is reduced in dorsal root ganglia neurons by high-frequency TENS in animals injected with the inflammatory irritant, formalin [17,86]. In

α-2a adrenergic knockout mice, antihyperalgesia by high-frequency TENS does not occur [54]. Blockade of peripheral, but not spinal or supraspinal, α-2 receptors prevents the antihyperalgesia produced by TENS [54], suggesting a role for peripheral α-2a-adrenergic in analgesia produced by TENS. Further, high-frequency TENS has effects on autonomic function and blood flow. Blood flow changes with high-frequency TENS are minimal and transient, with intensities tested always within the sensory range [16,20,91]. Thus, current evidence suggests that some of the analgesic effects of TENS are mediated through actions on primary afferent fibers and modulation of autonomic activity.

Low-Frequency (≤10 Hz) TENS

The antihyperalgesia produced by low-frequency TENS utilizes classic descending inhibitory pathways that include the PAG, RVM, and spinal cord [27,51,104]. Low-frequency TENS antihyperalgesia is prevented by blockade of μ-opioid receptors in the spinal cord or the RVM [51,104]. Furthermore, repeated application of low-frequency TENS produces tolerance to the antihyperalgesic effects of TENS and of spinal μ-opioid receptors [15], further supporting a role for μ-opioid receptors in TENS antihyperalgesia. The antihyperalgesia produced by low-frequency, sensory intensity TENS is also reduced by blockade of $GABA_A$, serotonin 5-HT_{2A} and 5-HT_3, and muscarinic M1 and M3 receptors in the spinal cord [64,79,81]. Similarly, serotonin is released during low-frequency TENS in animals with joint inflammation [106]. In monkeys, PET imaging studies show increases in the μ-opioid receptor in multiple regions of the cortex involved in pain processing in response to low-frequency TENS: anterior cingulate cortex, caudate, putamen, somatosensory cortex, and amygdala [123]. These changes were not observed with high-frequency TENS [123]. Studies in human subjects are consistent with this and show that low doses of naloxone, which would block μ-opioid receptors, prevent the analgesic effects of low-frequency TENS [100]. Taken together, these studies suggest that low-frequency TENS utilizes classical descending inhibitory pathways involving the PAG–RVM pathway, which utilizes opioid, GABA, serotonin, and muscarinic receptors in the spinal cord to reduce dorsal horn neuron activity, nociception, and the consequent pain.

Low-frequency TENS also has effects on the peripheral and autonomic nervous systems. Blockade of peripheral opioid receptors with naloxone at the site of application prevents the antihyperalgesic effects of low-frequency, but not high-frequency, TENS in an animal model of inflammatory pain [89], showing a role for peripheral opioid receptors in TENS analgesia. The reduction in cold

allodynia by low-frequency TENS is reduced by administration of systemic phentolamine to block α-adrenergic receptors [71]. In parallel, the antihyperalgesia produced by low-frequency TENS in animals with joint inflammation is reduced in α2A-noradrenergic receptor knockout mice, and prevented by peripheral blockade of α2-noradrenergic receptors (but not by spinal or supraspinal blockade) [54]. Blood flow changes, as a measure of autonomic activity, are mixed with small transient increases in blood flow in some cases with low-frequency TENS with intensities below or just above motor threshold. However, significant increases occur with stronger motor contractions greater than 25% above motor threshold [16,20,21,91,96]. Thus, peripheral effects of low-frequency TENS may involve changes in sympathetic activity utilizing local α2A-noradrenergic receptors, as well as μ-opioid receptors.

Electrode Placement

Few studies have addressed electrode placement. In one animal study, the effect of electrode placement was evaluated by placing electrodes within the receptive field for a spinothalamic tract neuron, outside the receptive field of the neuron but on the same limb, and at the mirror site [57]. The greatest degree of inhibition of spinothalamic tract cell activity occurred with electrodes placed within the receptive field for the neuron and only minimal inhibition occurred when placed on the same hind limb but outside the receptive field [57]. In animals with chronic muscle inflammation that results in bilateral hyperalgesia, electrode placement over the inflamed or the contralateral noninflamed muscle both reduced secondary hyperalgesia [2]. Similarly, in animals with acute cutaneous inflammation, application of TENS to the contralateral hind paw reduced primary hyperalgesia at the site of inflammation [89]. Together these data suggest that TENS produces a widespread analgesic response, that the greatest effect may occur if placed at the site of injury, but that application to the contralateral mirror-side may be effective in reducing hyperalgesia.

TRANSLATION OF MECHANISMS OF TENS ANALGESIA TO THE CLINIC

Clinically, TENS will more than likely not be the only treatment the patient is receiving. TENS is a complementary and adjunct treatment to control pain allowing the patient to engage in an active exercise program and return to

normal roles in society. Physical therapists who treat pain, particularly chronic pain, utilize a combination of exercise and functional training. Medically, the patient will more than likely be taking prescription and nonprescription medications such as nonsteroidal anti-inflammatories (NSAIDs), opioids (e.g., fentanyl, oxycodone, etc.), α-2 adrenergic agonists (e.g., clonidine), and/or muscle relaxants (e.g., cyclobenzaprine).

Parameters of stimulation of a particular modality, such as TENS, can be utilized in a more educated manner by applying basic knowledge. It has become increasingly clear that dosing (i.e., intensity of stimulation) is important for adequate effectiveness of TENS (for review [107]).

- The greatest analgesia is achieved with the highest tolerable dose [69,83]. There is a dose–response effect for TENS based on intensity. Doses at sensory threshold or below sensory threshold are ineffective.
- TENS produces the greatest effect while the unit is on and likely does not have long-lasting (weeks, months) effects [60,69]. Thus, one would expect that TENS could be used to modulate pain.
- TENS produces a reduction in movement-pain in those with musculoskeletal or acute pain conditions (postoperative, fibromyalgia, osteoarthritis) [22,56,84]. Minimal effects are observed in resting pain. Thus, use of TENS during exercise or activity may be more effective than while the person is at rest.
- TENS can alter pain physiology and thus targeting people with altered pain processing should result in the greatest effect. Specifically, because TENS increases central inhibition and reduces central excitability, application to people with alterations in pain physiology showing reduced central inhibition and greater central excitability could be more effective. This hypothesis was tested in a recent trial by examining the effects of TENS in people with fibromyalgia. In this group, TENS increased pain thresholds and restored central inhibition (conditioned pain modulation) [22].

Use of TENS (in combination with other therapies) will allow patients to increase their activity level, reduce hospital stay, and improve their function. Indeed, treatment with TENS increases joint function in patients with arthritis [1,55,65,66,126]. In patients with chronic low back pain, improvements on the physical and mental component summary on the SF-36 quality-of-life survey occur with TENS [35]. Postoperative TENS treatment in patients following thoracic surgery reduces recovery room stay and improves pulmonary function

as measured by postoperative PO_2, vital capacity, and functional residual capacity when compared with sham controls [3,84,120]. Thus, decreasing pain with TENS may increase function and allow the patient to tolerate other therapies and activities, resulting in an improved quality of life.

One should be aware of the medication a person is taking and the effects of these medications on the effects of TENS. If a patient is taking opioids (currently those available activate μ-opioid receptors), high-frequency TENS may be more appropriate. This recommendation is based on the fact that low-frequency, but not high-frequency, TENS is ineffective if given in animals tolerant to morphine [105]. Similarly, this frequency-dependent cross-tolerance of low-frequency TENS to opioid tolerance has been confirmed in people with chronic pain [59]. Specifically, in people with chronic pain who were tolerant to opioids, low-frequency TENS was ineffective but high-frequency TENS still reduced pain [59]. Thus, low-frequency TENS is ineffective if opioid tolerance (μ-receptor) is present.

Combining pharmaceutical interventions and TENS could enhance its analgesic effects clinically. Preclinical studies show that either high- or low-frequency TENS is more effective in reducing primary hyperalgesia if given in combination with acute administration of morphine [101] or clonidine [103] and should thus reduce the dosage of morphine or clonidine necessary to reduce hyperalgesia and the consequent side effects of the drug. Clinically, in patients using TENS, there is a reduction in the intake of opioids [35,87,109,110,119], and in nausea, dizziness, and pruritis associated with morphine intake [118]. Based on the known pharmacology presented above, one could hypothesize that selective serotonin reuptake inhibitors would prolong the effects of low-frequency TENS; combining NSAIDs with TENS could enhance the effectiveness of TENS; patients taking acetylcholinesterase inhibitors for cardiac disease might have a reduced effectiveness of TENS.

TOLERANCE AND TENS

As TENS is opioid mediated, it follows that repeated application of TENS would produce tolerance to its analgesic effects. In animals with joint inflammation, repeated daily application of either low- or high-frequency TENS is ineffective by the fourth day [15] (Fig. 11-5) and this tolerance is associated with a cross-tolerance at spinal opioid receptors. Pharmacological studies show that application of μ- and δ-opioid agonists simultaneously, blockade of *N*-methyl-D-

aspartate (NMDA) glutamate receptors, or blockade of cholecystokinin (CCK) receptors prevents development of tolerance to exogenous opioid agonists and thus similar strategies could be used to prevent tolerance to TENS. Pharmacologically, blockade of NMDA glutamate receptors or CCK receptors during application of TENS prevents the development of tolerance to either high- or low-frequency TENS (Fig. 11-5) [24,40]. In patients combining pharmacological treatments aimed at blocking NMDA receptors (i.e., ketamine or dextromethorphan) or CCK receptors (i.e., proglumide) with TENS could enhance the efficacy of TENS by prevention of tolerance.

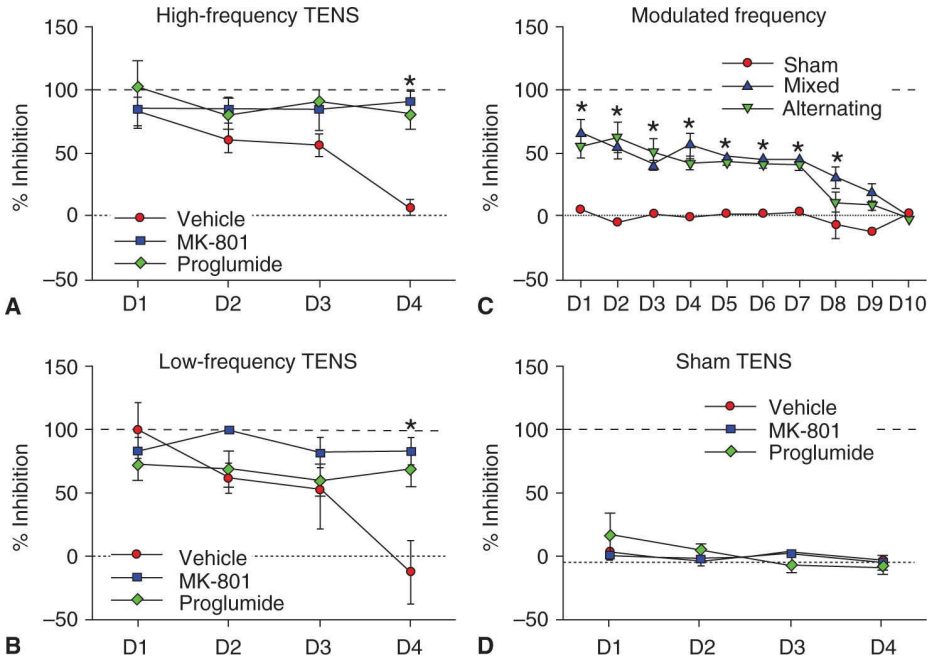

FIGURE 11-5 Graphs show the effects of repeated application of either high- or low-frequency TENS in animals that received a vehicle control **(A**, **B**, *red*) compared with those that received the NMDA antagonist MK-801 **(A**, **B**, *blue*), the CCK antagonist **(A**, **B**, *green*), or a combined application of low- and high-frequency TENS in the same session **(C**, mixed, *blue*) or alternating sessions **(C**, alternating, *green*). Withdrawal thresholds of the paw were measured before and after daily application of TENS to the inflamed knee joint (induced with 3% kaolin and carrageenan). Those that received sham TENS showed no change in withdrawal thresholds before or after treatment throughout the testing period. Notice the development of tolerance by day 4 in animals that received either **(A)** high-frequency or **(B)** low-frequency TENS and a vehicle (*red symbols*). In animals treated with MK-801 or proglumide, tolerance to either high- or low-frequency TENS did not develop. In those treated with mixed or alternating TENS, development of tolerance was significantly delayed. Data are represented

as a percentage change in hyperalgesia, induced by knee joint inflammation 24 hours earlier, before and after TENS on each day. Dotted lines represent no change in hyperalgesia (i.e., 0%). Hatched lines represent a complete reversal of hyperalgesia (i.e., 100%). Data are means +SEM. Asterisks (*) denote a significant increase from sham TENS in animals treated with vehicle. (Based on data from DeSantana et al. [24,26], Hingne and Sluka [40].)

Nonpharmacological approaches to prevention of tolerance by TENS have also been investigated. In animals with joint inflammation, simultaneous administration of low- and high-frequency TENS in the same session, or alternating administration of low- and high-frequency TENS on subsequent sessions, significantly delays the development of tolerance [26]. Further, increasing intensity by just 10% per day also delays tolerance to repeated application of either low- or high-frequency TENS [92]. A recent study shows that using mixed frequency with motor intensities produces the greatest delay in tolerance to TENS [62]. Thus, prevention of tolerance to TENS is critical for full effectiveness of treatment. Physical therapists can easily modulate frequencies of TENS in the clinic to prevent or delay the development of tolerance, and instructing subjects to increase intensity to maximal tolerable amounts can further obviate tolerance.

MECHANISMS OF IFT ANALGESIA

The mechanisms of action for IFT remain speculative at present. An animal study was able to show that IFT delivered at 4000 Hz carrier frequency, 140 Hz beat frequency with a pulse duration of 125 ms and pulse amplitude of 5 mA for 1 hour reduced spontaneous activity produced by formalin inflammation, and primary mechanical hyperalgesia produced by carrageenan inflammation [49].

CLINICAL EFFICACY OF TENS AND IFT

TENS

Although TENS is most commonly used for pain management, it has also been associated with non-analgesic effects such as antiemetic effects [50] and the promotion of wound healing [10]. In an attempt to highlight the limitations of

TENS clinical research to date, Table 11-2 summarizes key systematic reviews/meta-analyses that have been published on TENS. One of the key observations from this table is the small number of eligible randomized controlled trials (RCTs) that met the inclusion criteria for such reviews. In addition, lack of details of the TENS application, poor methodological quality of the trials, and heterogeneous study populations are all common problems specific to TENS research. Two recent commentaries and reviews describe methodological and interpretation concerns with systematic reviews. These reviews highlight the importance of dosing of the stimulation, timing of the outcome assessments, and appropriate subject selection. The reader is directed to these for a more in-depth review [6,107].

Several systematic reviews have reported negative or inconclusive findings for chronic pain conditions: knee osteoarthritis [88], cancer pain [12], poststroke shoulder pain [76], and chronic low back pain [52]. In contrast, Jin et al. [73] and Brosseau et al. [9] reported more positive findings for diabetic peripheral neuropathy and rheumatoid arthritis of the hand, respectively. Johnson and Martinson [45] published a meta-analysis on the efficacy of ENS for chronic musculoskeletal pain. The types of stimulation assessed were both TENS and percutaneous ENS and the range of conditions included rheumatoid arthritis, low back pain, osteoarthritis, ankylosing spondylitis, and myofascial trigger points. They included 38 studies in 29 papers for a total of 335 placebo, 474 ENS, and 418 crossover patients (both placebo and at least one ENS treatment). Data analyses of these studies indicated a significant decrease in pain with ENS compared with placebo. The authors highlighted that lack of statistical power was the main reason for disparity in their findings versus other studies and meta-analyses in this area.

Although TENS is commonly used as an intervention for chronic pain, its efficacy for acute pain conditions has also been examined: Simpson et al. [97] and [46] recently reported that TENS was effective for a range of acute pain conditions. Other systematic reviews have produced mixed results for postoperative pain [8,13], labor pain [14], and primary dysmenorrhea [78]. Bjordal et al.’s [8] meta-analysis on postoperative pain has highlighted the importance of considering the inclusion criteria in a meta-analysis or systematic review when interpreting the results. Bjordal et al. [8] only included those studies that used what they termed “optimal” stimulation parameters (i.e., appropriate dose), whereas Carroll et al.’s [13] earlier systematic review did not impose this as an inclusion criterion. Bjordal et al. [8] concluded that TENS can significantly reduce analgesic consumption for postoperative pain, whereas Carroll et al. [13] determined that the majority of studies they reviewed showed

no benefit for TENS. In recent years, more systematic reviews have utilized the Cochrane Collaboration's risk of bias tool to assess the methodological quality of RCTs [39]. This is a welcome transition for ensuring consistency across systematic reviews of electrotherapy.

TABLE 11-2 **Evidence for TENS Efficacy**

Disease/Pain Condition	References	Type of Review	Number of Studies	Results
Postoperative pain	[14]	Systematic review	17	Ineffective
Postoperative pain	[8]	Meta-analysis	21	Effective; adequate parameters necessary to get a positive effect
Post–thoracic surgery pain	[93]	Systematic review/ meta-analysis	11	Effective; TENS associated with pharmacological analgesia reduced pain compared with the placebo TENS associated with pharmacological analgesia (for sternotomy and thoracotomy)
Labor pain	[29]	Cochrane review	17	Limited evidence that TENS reduces pain in labor; it does not seem to have any impact (either positive or negative) on other outcomes for mothers or babies
Acute pain in the prehospital setting	[97]	Systematic review/ meta-analysis	4	Effective; TENS reduces severity of pain in patients with moderate-to-severe acute pain
Acute pain	[46]	Cochrane review	18	Effective; TENS reduces pain intensity greater than placebo (no current) TENS when administered as a stand-alone treatment
Knee osteoarthritis	[88]	Cochrane review	18	Inconclusive
Poststroke shoulder pain	[77]	Cochrane review	4	Inconclusive
Primary dysmenorrhea	[78]	Cochrane review	7	High-frequency TENS more effective than placebo; low-frequency TENS similar to placebo
Rheumatoid arthritis of the hand	[9]	Cochrane review	3	AL-TENS improved pain intensity and muscle power scores over placebo; C-TENS had no clinical benefit on pain intensity compared with placebo; C-TENS showed more clinical benefit on patient assessment of changes in disease over AL-TENS
Diabetic peripheral neuropathy	[44]	Meta-analysis	3	Effective; reductions in mean pain score were significantly greater in TENS group than in placebo TENS group at 4 and 6 weeks follow-up but not at 12 weeks follow-up

TABLE 11-2 **Evidence for TENS Efficacy (*continued*)**

Disease/Pain Condition	References	Type of Review	Number of Studies	Results
Dementia	[11]	Cochrane review	9	Inconclusive
Chronic musculoskeletal pain	[45]	Meta-analysis	38	Effective; concluded that prior studies had inadequate statistical power
Chronic low back pain	[53]	Cochrane review	4	Evidence does not support the use of TENS
Cancer pain	[42]	Cochrane review	3	Inconclusive
Phantom pain and stump pain	[70]	Cochrane review	0	No eligible RCTs found

Abbreviations: AL, acupuncture-like; C, conventional; TENS, transcutaneous electrical nerve stimulation.

As pain is multidimensional, assessment of other parameters may be equally important to measurement of pain at rest by a visual analog scale. DeSantana and colleagues [25,28] showed that TENS reduced both the affective and the sensory dimensions of pain, as measured by the McGill pain questionnaire, in patients with inguinal hernia surgery, and those undergoing sterilization procedures. Furthermore, pain with movement is particularly problematic postoperatively, and likely represents a form of hyperalgesia. Rakel and Franz [84] reported that in people recovering from abdominal surgery, pain with walking or deep breathing was significantly reduced by high-frequency TENS. However, they showed no effect on pain at rest [84]. Similarly, in people with fibromyalgia, Dailey et al. [22] showed a reduction in pain during the 6-minute walk test but not at rest during high-frequency TENS.

Last, recent evidence supports the importance of adequate dosing, in particular for pulse amplitude. In an experimental pain study, Rakel et al. [83] showed that increases in pressure pain threshold (PPT) and reductions in temporal summation in healthy volunteers occurred with pulse amplitudes greater than 17 mA when compared with a placebo. Pulse amplitudes below 17 mA showed no significant changes in PPT or temporal summation. Similarly, Bjordal et al. [8] and Rakel and Franz [84] showed that TENS was only effective if given at pulse amplitudes greater than 12 or 9 mA, respectively, in people with postoperative pain. Moran et al. [69] confirmed a dose–response hypoalgesic effect of TENS in healthy controls with the largest hypoalgesic effect occurring with the highest pulse amplitudes. Pantaleão et al. [75] demonstrated that adjusting the pulse amplitude to maintain a strong but comfortable intensity during TENS application produced greater hypoalgesia in healthy volunteers compared with not adjusting the pulse amplitude. Recently, Dailey et al. [22] employed this combination of using relatively high pulse amplitudes to produce and maintain maximal tolerable intensities in a crossover RCT of 43 patients

with fibromyalgia. TENS applied in this manner for 30 minutes produced a significant decrease in pain and fatigue with movement compared with placebo and no TENS applications.

From the current literature on TENS, it can be concluded that further evidence is required on its efficacy, parameter-specific effects, and indeed cost-effectiveness. Optimal stimulation parameters and treatment durations should be considered while interpreting the outcome of systematic reviews and meta-analyses on TENS.

IFT

Traditionally, IFT was applied in a physical therapy clinic, which limited its use for different pain conditions. However, small portable IFT units are now widely available (see Fig. 11-2), which allows IFT to be applied for similar pain conditions to TENS. The main clinical indications for using IFT are pain management [23], reduction of swelling [43], and muscle strengthening [7,113]. In a postal survey of 416 physical therapists in the United Kingdom and Hong Kong on the use of TENS for pain management, Hong Kong physical therapists reported using TENS and IFT more frequently than their UK colleagues [94]. When asked to rate the perceived effectiveness of the two modalities for acute and chronic pain, both groups indicated that IFT was more effective for acute pain. However, Hong Kong physical therapists rated IFT more effective for chronic pain whereas UK physical therapists felt TENS was more effective. Poitras et al. [76] highlighted the popularity of IFT in physical therapy clinics in Canada for low back pain, and a further two surveys have reported that IFT was the most widely used electrotherapeutic modality for this condition in the UK and Ireland [31,37].

Experimental pain models show no consistent effect of IFT for measures of cold pain, ischemic pain, delayed-onset muscle soreness, or PPT [4,47,48,68]. In terms of clinical efficacy, no Cochrane reviews have been published on the effectiveness of IFT for pain. However, Fuentes et al. [32] published a recent systematic review and meta-analysis on the effect of IFT for musculoskeletal pain. Twenty RCTs met the inclusion criteria and comprised trials on joint pain, muscle pain, postoperative pain, and soft tissue shoulder pain. The authors indicated that heterogeneity across the studies and methodological limitations prevented conclusive statements regarding the analgesic efficacy of IFT; only three RCTS were considered to be of high methodological quality.

Hurley et al. [41] showed that for acute back pain, IFT alone, manipulative therapy alone, or IFT and manipulative therapy combined produced

improvements in functional disability, pain, quality of life, analgesic medication consumption, and exercise participation (up to 12 months). Although improvements were noted in all three treatment groups, there were no significant differences between the groups. IFT was applied using two electrodes applied over the appropriate spinal nerve roots (3.85 kHz carrier frequency, 140 Hz beat frequency); participants received an average of five physiotherapy treatments over a period of 5 weeks. There was no placebo control in this study.

Zambito et al. [125] compared the effects of IFT (200 Hz modulated beat frequency, dermatome application, 10 minutes, 5× per week for 2 weeks), horizontal therapy (HT, a form of electrical stimulation), and sham HT groups in a sample of patients with multiple vertebral compression fractures or degenerative disk disease. In another study on multiple vertebral compression fractures, Zambito et al. [124] again compared IFT (treatment as above except that duration was 30 minutes duration) with HT or sham HT groups. Results from these two studies showed a significant reduction in pain in both HT and IFT groups compared with the sham HT group at weeks 6 and 14. In both of the above studies, all treatment groups did flexion and extension stretching exercises for the same 2-week duration as the IFT/HT.

In people with knee osteoarthritis, Defrin et al. [23] demonstrated that IFT delivered with a carrier frequency of 4000 Hz (20 minutes applied on 12 occasions) reduced pain and morning stiffness compared with sham and control groups. Pain was reduced if the IFT was delivered at either a noxious (30% above pain threshold) or an innocuous intensity level (30% below pain threshold). This study also reported no significant differences in treatment outcomes if the patients routinely adjusted the pulse amplitude to prevent the sensation fading versus those patients who did not adjust the pulse amplitude even though the sensation was fading. This was the first study to clinically examine the concept of accommodation associated with the application of electrical currents. More recently, Atamaz et al. [5] compared the effects of active TENS (80 Hz, 20 minutes), active IFT (100 Hz, 20 minutes), active shortwave diathermy with sham interventions of all three types of therapy in an RCT of 203 patients with knee osteoarthritis. All patients received their allocated therapy 5× a week for 3 weeks in addition to an education program and exercises. Compared with baseline data, there was a significant decrease in knee pain, time to walk a distance of 15 m, and paracetamol intake in all groups but no significant difference among the groups. The only significant finding between each active therapy and its respective sham therapy group was for the intake of paracetamol. The intake of paracetamol was significantly lower in each treatment group when compared with its respective sham group at 3 months. In

addition, the patients in the IFT group used a significantly lower amount of paracetamol at 6 months in comparison with the IFT sham group.

Suriya-Amarit et al. [112] compared 20 minutes of IFT (100 Hz) with 20 minutes of placebo in an RCT of 30 patients with hemiplegic shoulder pain. Participants who received IFT reported a significantly greater reduction in pain during the most painful shoulder movement than those in the placebo IFT group. In addition, the IFT group showed a greater improvement in posttreatment pain-free passive range of movement than the placebo group in shoulder flexion, abduction, internal rotation, and external rotation.

Thus, there is emerging evidence from RCTs that IFT is effective for reduction of pain associated with knee osteoarthritis, degenerative disc disease or vertebral fractures, and hemiplegic shoulder pain. However, more placebo-controlled RCTS and systematic reviews are required to determine the clinical efficacy of IFT.

SUMMARY

In summary, there is evidence from basic science, as well as clinical studies, that TENS is an effective treatment for the control of both acute and chronic pain conditions. Evidence suggests that frequency of stimulation activates different endogenous analgesia systems, and that intensity of stimulation is critical to pain relief. For IFT, evidence is emerging from RCTs to support its use. However, the mechanisms by which IFT produces its analgesic effect are unknown.

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CHAPTER 12

Overview of Other Electrophysical Agents Including Thermal Modalities

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The roles of TENS (transcutaneous electrical nerve stimulation) and IFT were reviewed in the previous chapter. The focus of this chapter is on the analgesic capabilities of the other commonly used agents, whether these be purely thermal (e.g., hot and cold packs), sound based (ultrasound), or electromagnetic (shortwave diathermy [SWD], low-level laser therapy, or photobiomodulation [PBm]). Principles of application will be minimally addressed as it is expected that the reader is generally familiar with these issues. The chapter will focus on relevant mechanisms of action and current evidence of clinical effectiveness for each agent. A detailed examination of the principles of application for each of these modalities is beyond the scope of the current chapter; for these the reader is directed to some of the specialist texts available [2,3,47,70]. In particular, in using thermal modalities, a thorough understanding of the contraindications and precautions is essential given the risk of burns or scalds; further details on these are presented elsewhere (e.g., reference [5]).

THERMOTHERAPY

The analgesic capabilities of the thermal agents (i.e., heat and cold) are widely accepted and have been known since antiquity. All rely on only three processes: conduction (hot and cold packs), convection (whirlpool baths), and conversion of another form of energy to heat (ultrasound and SWD). The latter are the only modalities capable of heating deeper seated structures and tissues. Although a wide variety of agents is available, this chapter will concentrate on hot packs, SWD, ultrasound, and ice therapy as they represent the most popular forms of thermotherapy [69].

Hot Packs

Hot packs are a popular choice for the relief of pain on the basis of their cost-effectiveness and ease of use [2]. Packs used in physical therapy are usually kept suspended in hot water baths at temperatures ≤80°C and are drained and wrapped in toweling prior to patient application. Application time is typically up to 20 minutes, limited by patient tolerance and cooling of the pack. Packs for patient self-use are widely marketed and are typically designed to be heated in a microwave oven prior to use; alternative forms of conductive heating also available include electrical heating pads and hot water bottles.

Shortwave Diathermy

SWD machines are transmitters that produce electromagnetic radiation within the radiofrequency range (regulated to operate at a frequency of 27.12 MHz). Operation can be continuous (where the aim is to cause tissue heating) or pulsed, usually with the aim of producing nonthermal effects (also called *pulsed electromagnetic energy*). Treatments are based on tuning the circuit (comprising the patient and the machine) in a similar fashion to a radio set; this is now automatically done by the machine on contemporary units. Once this is completed, treatments usually last for up to 20–30 minutes, during which patient feedback is used to monitor treatment. Contemporary units include a base unit, along with applicators, which may comprise pairs of electrodes (for capacitive treatments), or pads or arm-mounted drums (for inductive applications); rubber-coated cables as applicators (coiled over or around a body part), although once popular, are now rarely used because of concerns about an increased risk of overheating and prolonged setup time.

Tissue heating with continuous SWD can be significant (6°–15°C depending on depth and type of tissue) and is produced by electrical “eddy” currents (when inductive application is used) or electrical fields (capacitive application) within the tissue [23,50]. The former predominantly causes heating of muscle tissue (through the tissues’ resistance to the current), whereas the latter produces relatively more heating in structures such as ligaments, tendons, and joint capsules (through continuously reversing field polarity) [23,50]; this is an important consideration in targeting the treatment to a particular anatomical site of pain (e.g., tendonopathy vs. myogenic pain).

Cold Therapy (Cryotherapy)

A variety of means are used to provide cold therapy or cryotherapy: These include relatively simple ice packs (i.e., bags filled with crushed ice from an ice machine), ice massage, or packs of frozen peas, as well as the more sophisticated (and expensive) gel-filled packs. Apart from ice massage, which is typically applied directly to the skin using paper/Styrofoam cups in which water has been frozen and the top peeled away to expose the ice, a wet towel is usually employed as a barrier between the pack and the skin to prevent ice burn. In some cases, oil may also be lightly applied to the skin to reduce such risk.

A range of alternative cooling media is also available. Examples include vapocoolant sprays and chemical "break and apply" packs; however, for routine use these do not seem to offer any additional benefit over ice application, and some may indeed be less efficient in cooling treated tissues [14,45,59].

Although cryotherapy is by its nature a superficial thermal modality, its physiological and (thus) clinical effects can be significant and systemic. Cryotherapy produces a rapid vasoconstriction in superficial tissues (after 5 minutes of cooling), which becomes evident in deeper tissues (including periarticular structures, muscle, and bone) after 20 minutes of application [1,41,59]. Although treatments may last for up to 20–25 minutes, cryotherapy using ice can produce localized analgesia within a much shorter period when applied directly over the site of pain (reported by the patient as "numbness" after 10 minutes or less). Apart from significant changes in skin temperature during treatment (e.g., up to 20°C in some cases), temperature changes in deeper seated structures can also be profound: ice treatment in osteoarthritic knee joints was found to reduce intra-articular temperatures by 6°C [12,45,59].

Mechanisms of Pain Relief with Thermal Modalities

Thermotherapies achieve their clinical effects by changing tissue temperatures, which in turn effect alterations in cellular and physiological function. Both heat packs and cold packs increase pain thresholds in healthy controls. The effects of thermal modalities for pain reduction are aimed at reducing the activation of nociceptors in the periphery, and thus their effects are mostly at the peripheral sites. Although changes in temperature produced during treatment may in some circumstances be relatively modest (around 5°C or less), the effects upon cellular and physiological functions such as nerve conduction or blood flow can be significant; furthermore, effects—particularly in terms of blood flow—may affect distal parts of the body [1,20,48,49]. Altered nerve conduction and changes in blood flow are considered to be particularly important in terms of the pain-relieving effects of heat and cold [1,48,49]. Changes in blood flow are

likely to improve tissue healing, to remove inflammatory irritants and consequently decrease activity of nociceptive afferents to ultimately decrease pain. Ice clearly decreases conduction velocity of primary afferent fibers; if the temperature reaches 4°C, conduction of afferent fibers is stopped. Decreasing conduction velocity of afferent fibers thus would produce analgesia by decreasing firing of afferent fibers and consequently decreasing input to the central nervous system.

Heat has long been employed by physiotherapists to help mobilize tissues and joints by increasing tissue extensibility and reducing muscle spasm. This would be expected to remove mechanical irritants from nociceptors and decrease input to the central nervous system. Heat-induced alterations in muscle spindle activity and in firing of Golgi tendon organs are thought to be responsible for the observed reductions in muscle tone [56]. Type II spindle afferent fibers show a reduced activity after heating whereas Type I spindle afferent fibers show an increased activity. As Type II spindle afferents monitor muscle length, decreased activity should result in decreased activity of the α-motor neuron to decrease muscle spasm. A concomitant increase in Golgi tendon organ firing would also decrease α-motor neuron firing through an interneuron circuit in the spinal cord. Joint stiffness as a feature of inflammatory arthritis (and some other forms of arthrogenic pain and joint irritability) can be reduced with heating [73]. Although cooling can have similar effects to heating in terms of reducing muscle tone or spasticity [1,36,57], it can also increase stiffness—at least in the small joints of the hand [43,73].

Effectiveness of Heat and Cold Therapy

The evidence base to support the use of thermal modalities in the alleviation of pain is limited by the quality of a number of relatively dated investigations. Most of the studies to date have been completed on musculoskeletal pain, including low back and arthritic pain; previous Cochrane reviews in these areas have indicated potential benefits of superficial heat and cold [12,15,31,63]. In the management of rheumatoid arthritis, no differences were found between effectiveness of (or patient preference for) most types of thermotherapy; superficial heat and cryotherapy were recommended for use as palliative therapy and wax/paraffin baths with exercises for short-term effects for arthritic hands [63]. In osteoarthritis, ice packs may provide benefits in terms of swelling and range of movement but appear ineffective in terms of pain [12]. For low back pain, a review of the effectiveness of superficial heat found moderate evidence of short-term reductions in pain in cases of acute or subacute low back pain;

there was insufficient evidence to assess the effectiveness of cryotherapy [31,61].

Ice has long been recognized—by clinicians and the public alike—as an important component of the RICE management of musculoskeletal injuries in the acute stage (i.e., Rest, Ice, Compression, and Elevation). A previous review of the evidence of effectiveness of ice and compression in acute soft tissue injuries found only limited evidence of effectiveness [10]; a more recent review found immersion cryotherapy effective in reducing delayed onset muscle soreness [9].

A recent review of superficial cooling for postpartum perineal pain found limited evidence of reductions in pain in the short term following local cooling treatments (i.e., ice packs, cold gel pads, cold/iced baths) [28].

Despite an extensive history of clinical use of SWD for alleviation of musculoskeletal pain, the evidence base for such use is limited and contradictory: Whereas one recent controlled trial of continuous SWD in knee osteoarthritis found significant reductions in pain [44], another reported no additional benefit (albeit with pulsed treatment) for back pain [27].

Ultrasound

Ultrasound has been used for decades [2]. Contemporary machines combine a base or controller unit, which allows the operator to select treatment parameters (typically treatment time, continuous wave or pulsed operation, and intensity in W/cm^{-2}), and treatment applicators operating at fixed pulsing frequencies. Increasingly sophisticated units have become more popular in recent years, providing basic clinical decision-support and parameter selection systems. Patient treatment involves moving the ultrasound applicator over the painful area or lesion, using a circular or back-and-forward motion, and water-based gel as a coupling medium; for more-difficult-to-treat areas (such as the small joints of the hands) the applicator and the limb to be treated may be both immersed in a water bath filled with degassed water. Treatment times are typically 5–10 minutes.

Ultrasound is a form of mechanical energy, comprising alternating compressions and rarefactions of the medium, at frequencies above the (human) audible range. Typical ultrasound frequencies range from 0.8 to 3 MHz (c.f., upper limit of audible range c. 20 kHz) and share common physical properties with sound energy. Depending on the parameters used, ultrasound may produce thermal or nonthermal effects; higher power intensities and continuous wave operation are more commonly used in North America (e.g., compared with the

United Kingdom) to provide thermal effects including increased blood flow and soft tissue extensibility, as well as for pain relief, possibly linked to reported effects on peripheral nerve function [19,62]. A variety of other effects predominate at nonthermal intensities (typically <0.5 W/cm^{-2} and using pulsed mode), including cavitation ("bubble formation"), acoustic streaming, and deformation of the insonated tissue (i.e., the transmission media). The primary goal of treatment at such nonthermal intensities is promotion of tissue repair processes through enhanced cellular function and metabolic processes [24–26,58].

Whereas intensity (specified in W/cm^{-2}) is an important parameter in determining the amount of heating produced, the frequency of the ultrasound determines its depth of penetration and is thus an important parameter in targeting treatment to particular anatomical structures. Higher frequencies (e.g., 3.0 MHz) are used for the treatment of more superficial tissues (up to 2 cm deep; e.g., superficial paraspinal musculature), whereas lower frequencies (≤1.0 MHz) are employed for more deeply seated structures or lesions [35]. Tissue type and orientation also determine penetration, with ultrasound penetrating fat and muscle more readily than bone [33,51,53,71].

Temperature changes resulting from ultrasound treatment can be significant (5°–10°C) and may be most pronounced at interfaces between tissues with different transmission characteristics (e.g., bone–muscle) [51,52]. Thus, although the depth and uneven aspects of ultrasound heating are a concern, the safety concerns related to ultrasound are primarily those associated with other forms of heating. However, even at nonthermal intensities, mechanical effects of ultrasound (e.g., cavitation) can be potentially damaging, and thus sensitive structures such as the eyes are avoided as well as treatment over the pregnant uterus, heart, brain, and cervical ganglia. Caution should also be exercised with treatment of the back, avoiding the use of high intensities over the spine, and direct treatment over laminectomy or surgical sites with metal implants has long been recognized as a (prudent) contraindication [34]. Although ultrasound therapy has found popular application in the treatment of arthrogenic pain, as with other forms of heating, its use at thermal intensities should be avoided in younger people with immature growth plates, as well as in acute exacerbations of inflammatory disease or over inflamed joints, as it may exacerbate the inflammatory process [52,72].

Effectiveness

Despite long-standing and widespread use in musculoskeletal physical therapy,

research findings to support the use of ultrasound for the treatment of pain are limited and inconclusive [13,18,40,63]. In particular, the Philadelphia Panel's evidence-based guidelines for musculoskeletal rehabilitation reported that although there was evidence of benefit in ultrasound of some shoulder disorders (calcific tendonitis) [29], there was no convincing evidence of benefit in the treatment of musculoskeletal pain of other aetiologies [40]. Review of research findings for different interventions in the treatment of heel pain found no convincing evidence of benefit of therapeutic ultrasound [18]. A randomized controlled trial in lateral epicondylalgia found continuous wave ultrasound offered better pain relief than did rest, but was no more effective than sham treatment [54]; a subsequent study using pulsed ultrasound reported similar results [39]. More recent work, as part of two small-scale controlled studies on myofascial trigger points, found low-intensity ultrasound to be effective in desensitizing in trapezius and infraspinatus trigger points [65,66].

A Cochrane review of thermotherapies found no significant clinical benefit of therapeutic ultrasound in the treatment of rheumatoid arthritis [63]; however, a more focused review of ultrasound treatment reported a range of benefits (including reduced early morning stiffness and increased range of motion) in the treatment of rheumatoid hands, which is also supported by the recommendations of the Ottawa Panel on electrophysical agents for treatment of rheumatoid arthritis [13,60]. A more recent review has highlighted a range of potential benefits in osteoarthritis, including pain relief [64].

Neurogenic pains, and particularly postherpetic neuralgia, have been treated with therapeutic ultrasound, apparently with some success [32,68]; however, published studies are rather dated, poorly controlled, and contradictory.

Low-Level Laser Therapy or Photobiomodulation Therapy

Since initial reports first appeared in the late 1960s and early 1970s, low-power laser devices have found a range of treatment applications in physical therapy, primarily to accelerate tissue healing, in conditions ranging from chronic ulcers to soft tissue injuries [3]. Such devices have also been used in the management of pain of various etiologies, although, as is true of wound healing, such use has been contentious [21]. Since the 1980s, most devices used in physiotherapy have been diode-based systems (rather than the former helium–neon gas-based systems), comprising either single (laser/diode) source treatment applicators, or —increasingly—multidiode arrays comprising up to several hundred (laser and superluminous monochromatic) diodes [3]. Device outputs can vary from less than 10 mW to several hundred mW; however, recent times have seen higher

outputs as the norm (at least >30 mW). Most systems produce radiation at single wavelengths between the visible red to near-infrared part of the spectrum (i.e., around 630–904 nm), although for pain relief and musculoskeletal (i.e., non–wound healing) applications, use of infrared wavelengths is the norm. Treatment dosages used for treatment of musculoskeletal pain have been variable; however, suggested irradiation parameters for a range of tendinopathies and arthritic conditions are available from the World Association for Laser Therapy (WALT) website (see http://waltza.co.za/documentation-links/recommendations/). Treatments usually consist of application of laser to localized areas of tenderness and pain in a grid (or sweeping) pattern, as well as the irradiation of acupuncture or trigger points.

The mechanisms underpinning the observed pain-relieving effects of laser therapy have been debated for some years and remain arguable in some quarters; however, a review of neurophysiological investigations in human and animals found consistent evidence of inhibitory effects of laser irradiation, at least in the peripheral nervous system [16].

Studies over many years in animal models of pain have typically reported significant pain-relieving or antinociceptive effects of laser irradiation, which are dependent on the parameters used (e.g., reference [42]). Such effects are apparently based on a variety of neuropharmacological mechanisms, which may be opiate mediated [30].

Unlike the modalities considered above, laser therapy as currently used is essentially athermic (nonheating), and thus safety considerations are less onerous. In particular, laser therapy can be used in many cases for the treatment of acute pain or injury, without the risk of exacerbation of the inflammatory process. This, however, does not always apply to some of the higher output units that have become more commonly used in more recent years: These incorporate defocussed higher outputs sources and may produce heating. The operator should confirm the output of the system in use, and thus the potential heating effects of the device. Other safety considerations and contraindications are associated with the (minor) risk to the unprotected eye, and application in cases of active or suspected carcinoma [5].

Effectiveness

The effectiveness of laser therapy for alleviation of pain has previously been a matter of debate, in part because of dispute over the putative mechanism of action [4,21]. Systematic reviews of clinical effectiveness have found laser therapy to provide clinically significant benefits in chronic joint pain [6], in the

osteoarthritic knee [7], for short-term alleviation of pain and morning stiffness in rheumatoid arthritis [11], and for neck pain [17]. Additionally, a review of physical therapies for temporomandibular joint pain found that laser therapy was effective, and apparently more effective than other electrophysical agents [55]. In other conditions, the evidence is less clear: For shoulder pain, adhesive capsulitis is the only condition for which laser therapy has shown benefit [37]. Although previous reviews have reported no convincing evidence of benefit of laser therapy in lateral epicondylitis, a more recent review and meta-analysis found short-term pain relief with laser treatment at some wavelengths (principally 904 nm) [8,67]. The most recent review of laser therapy for treatment of low back pain reported that there was insufficient evidence to draw any conclusions on potential benefits [74].

TABLE 12-1 **Table of Evidence for Heat, Cold, Ultrasound, and Laser Therapy**

Disease/Pain Condition	References	Type of Review	Number of Studies	Results
Low back pain	[15]	American Pain Society Guidelines	Based on systematic reviews	Superficial heat is effective for acute low back pain
Low back pain	[31]	Systematic review	*n* = 9	Heat wrap therapy (superficial heat) effective for acute and subacute low back pain (moderate evidence); additional benefit when combined with exercise. Insufficient evidence to evaluate cold therapy
Rheumatoid arthritis	[63]	Cochrane review	*n* = 7	Superficial moist heat and cryotherapy can be used as palliative care. Wax baths combined with exercise provide short-term benefits in arthritic hands
Rheumatoid arthritis	[60]	Ottawa Panel guidelines	*n* = 5 PBM; *n* = 1 US; *n* = 2 thermal	Recommended PBM, US, and thermotherapy
Osteoarthritis	[63]	Cochrane review	*n* = 3	Cold therapy improved ROM, function, knee strength, and reduced edema; cold therapy had no effect on pain; superficial heat had no effect on edema
Osteoarthritis of the knee	[7]	Systematic review	*n* = 8	PBM administered with optimal doses offers clinically relevant short-term pain relief for OA knee
Acute soft tissue injury	[10]	Systematic review	*n* = 22	Ice plus exercise is effective (marginal evidence)
Delayed muscle soreness	[9]	Systematic review	*n* = 17	Immersion cryotherapy may reduce soreness following exercise
Musculoskeletal pain	[40/29]	Philadelphia Panel guidelines	Unclear	Recommended ultrasound for calcific tendonitis of the shoulder
Chronic joint pain	[6]	Systematic review	*n* = 11	PBM effective in reducing joint pain with appropriate dosages
Neck pain	[17]	Systematic review	*n* = 16	PBM effective in reducing pain for up to 22 weeks
Myofascial trigger points	[46]	Systematic review	*n* = 49	Laser acupuncture in managing musculoskeletal pain when applied in an appropriate treatment dosage; positive effects are seen at long-term follow-up and not immediately after the cessation of treatment

Abbreviations: PBM, photobiomodulation/low-level laser therapy; US, ultrasound; ROM, range of motion.

Clinical trials in other conditions have reported potential benefits of laser therapy in the treatment of fibromyalgia [38], and as an adjunctive treatment when combined with exercise in the management of chronic low back pain [22]. For laser acupuncture (the use of laser as an alternative to needle for acupuncture treatments), a recent review and meta-analysis found evidence of benefit in several forms of pain [46].

In the United States, since relaxation of registration requirements, the Federal Food and Drug Administration (FDA) has approved more than 25

different laser therapy devices for the treatment of pain since 2002 (Table 12-1) [2].

SUMMARY

These agents, in addition to TENS and IFC as discussed in Chapter 7, are important considerations for the treatment of a patient's pain. Nevertheless, a number of caveats are in order. First, the evidence base for the effectiveness of these agents, particularly for anything more than short-term pain relief, is somewhat limited. Second, with the exception of the tissue-penetrating capabilities of agents such as ultrasound and the diathermies, there is little evidence that the newer modalities are any more effective than the old standbys of heat and cold. Third, although not emphasized in this presentation, while some of these approaches (e.g., TENS) may be used in isolation, they are almost always most beneficial as adjuncts to a program focused on exercise, strengthening, mobilization, and education. And fourth, choice of treatment depends on a combination of the etiology of the pain, treatment goals, duration (e.g., ice for acute musculoskeletal injury), area to be covered (ultrasound for limited areas, hot packs for wider areas), intensity (ice massage vs. cool packs), and depth (ultrasound vs. hot packs).

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CHAPTER 13

Manual Therapy

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MANUAL THERAPY TECHNIQUES

Dependent on the nature of the presenting clinical disorder contemporary manual therapy will utilize detailed information derived from the subjective and physical examinations to plan and offer various clinical interventions. Such manual therapy techniques may include traditional massage, soft tissue mobilization, joint mobilizations and manipulations, nerve or "neural" mobilization procedures, joint stabilization exercises, self-mobilization exercise, and importantly patient advice for appropriate self-management strategies as well as devising strategies for reducing risk of injury recurrence.

Traditional massage includes techniques such as effleurage and petrissage that are delivered to the body part affected. Massage is typically applied to relieve muscle and soft tissue tightness and reduce pain. Soft tissue mobilization techniques involve sustained stretching of the muscle or connective tissue and are similarly used to reduce soft tissue tightness and pain. These include trigger point therapy, myofascial therapy, or deep tissue massage. Neural mobilization is a technique designed to restore the ability of the nerve and surrounding structures to shift in relation to surrounding structures by putting the nerve and its surrounding tissue in a stretched position. Joint mobilizations are used to describe movement of joints that either apply sustained positions, or oscillatory repetitive movements with the normal physiological range. Mobilizations have been graded from I to IV, with Grade I described as an oscillation at the beginning of range, II within mid-range, III to end of range, and IV within the end of range for the joint. Manipulations are generally high-velocity, low-amplitude movements of a joint, sometimes termed type V manipulation/mobilization. This chapter will review the basic science mechanisms underlying these types of treatments, and the clinical evidence to support their use for common pain conditions.

BASIC SCIENCE MECHANISMS

Massage

The basic science mechanisms underlying massage have included evidence aimed at deciphering central pathways activated by massage. In addition several theories are used to support its use. In an animal model used to decipher the mechanism of massage, 10 minutes of massage to the abdomen increases pain thresholds, with increasing pain thresholds observed as a cumulative effect from an increased number of daily treatments [26]. In this model, the neuropeptide oxytocin increases in the plasma and periaqueductal gray (PAG) in the midbrain in response to the massage treatment when compared with a control treatment [26]. This model is supported by the observation of a reduced analgesic effect from massage when oxytocin receptors are blocked, either systemically or in the PAG [2]. Studies in human subjects also show that massage decreases pain intensity and simultaneously decreases cortisol in the blood in people with juvenile rheumatoid arthritis or burn injury [15,16]. However, the effects on cortisol are small and may not be clinically significant [32]. An increase in plasma serotonin has also been observed in response to massage in people with either burn injury or migraine [15]. Thus, massage may activate descending inhibitory pathways that include the PAG using oxytocin and possibly serotonergic systems to produce analgesia.

Peripherally, massage can promote healing by directly reducing expression of inflammatory genes and cytokines and increasing genes involved in healing. Using delayed onset muscle soreness, which is induced by eccentric exercise, as a model of muscle pain and injury, deep tissue massage reduces pain during stretch and both superficial touch and deep tissue massage reduce mechanical hyperalgesia in people with delayed onset muscle soreness [17]. In healthy individuals with delayed onset muscle soreness, deep tissue massage upregulated PGC-1a, a mediator of tissue repair and metabolic control involved in mitochondrial biogenesis, and decreased nuclear factor κB (NF-κB) (which plays a critical role in muscle inflammation), phosphorylation of heat shock protein 27 (HSP27) signaling (which is an indicator of intracellular stress), and inflammatory cytokines IL-6 and TNF-α (which by themselves activate nociceptors and produce pain) [9].

Theoretically massage could also produce its pain-relieving effects indirectly by helping to restore normal movement patterns through connective tissue remodeling and reduction in connective tissue tension. While the extracellular

matrix composition and organization is involved in this process, the fibroblasts may also be actively involved. Loose connective tissue forms a network of fascia that separates muscles and organs throughout the body and consists of irregularly woven collagen fibers. Loosely arranged connective tissue is actively remodeled in response to changes in tissue length. Fibroblasts produce the collagen that forms the extracellular matrix, and in loose connective tissue their function is modifiable. Specifically, fibroblasts adjust to tissue length by static stretch changes, the morphological response of fibroblasts adopting a larger, more spread-out morphology, which may give loose connective tissue its compliant and viscous properties [1]. Increases in extracellular ATP occur in response to static stretch of fibroblasts, and the increase in fibroblast area is prevented by blockade of purinergic (P2X) receptors [21]. In an animal model of low back pain induced by carrageenan inflammation, tissue stretch 10 min/d for 12 days improved altered gait decreased mechanical hyperalgesia, and reduced macrophage infiltration in the connective tissue [8]. Thus, manual therapy can reduce hyperalgesia by altering connective tissue morphology and reduce infiltration of macrophages.

In summary, massage has multiple potential mechanisms of action and results in reduced pain and hyperalgesia. Massage reduces stress and may reduce cortisol levels, alters neurotransmitter release in the central nervous system, and activates descending inhibitory systems. Peripherally, massage can alter gene transcription in the muscle to promote healing and reduce inflammation, alter connective tissue morphology, and reduce infiltration of inflammatory cells. Thus, massage could also produce its pain-relieving effects indirectly by helping to restore normal movement patterns, reduce muscle spasms, and improve healing to reduce mechanical or chemical irritants that activate nociceptors and simultaneously activate central inhibitory mechanisms to consequently reduce pain.

Joint Mobilization and Manipulation

Joint manipulation and mobilization have been shown to produce effects both peripherally and centrally. Peripherally, high-thrust manipulation and mobilizations increase pain thresholds and decreases motor neuron excitability as measured by the H-reflex in human subjects [3,5,10,19]. This reduction in motor neuron excitability is short lasting, approximately 10–20 seconds in healthy controls. However, in people with low back pain, spinal manipulation increases the activity of the oblique abdominal muscle, but has no effect in normal healthy controls [13], suggesting longer term effects on motor neuron

excitability in people with chronic pain. In an animal model, at the time of a lumbar spinal thrust a reduction in activity of muscle spindle afferent fibers that lasts for several seconds has been observed [43]. This reduction in muscle spindle activity is accompanied by a decrease in EMG activity in the paraspinal muscles that lasts for at least the duration of the recording period, approximately 6 minutes [37]. Thus, peripherally, spinal manipulation can decrease muscle spindle activity, reduce motor neuron excitability, and reduce EMG activity of the paraspinal muscles and would therefore be expected to decrease muscle spasm of the paraspinal musculature. Decreasing the muscle spasm would then be expected to decrease muscle ischemia and thus nociceptor sensitization to reduce central input to the spinal dorsal horn.

Joint mobilizations of the cervical spine (Grade III lateral glide of C5/6) increase pressure pain thresholds, increase pain-free range of motion for the upper limb tension test, and increase pain-free grip force in people with lateral epicondylalgia [45]. In people with knee osteoarthritis, application of joint mobilization procedures has demonstrated an increase in pressure pain thresholds at the knee and the heel, suggesting a reduction in both primary and secondary hyperalgesia [31]. Furthermore, there is an immediate decrease in temporal summation following spinal manipulation in healthy individuals and in individuals with chronic low back pain, suggesting central mechanisms may play a role [3,19] (Fig. 13-1). In animal models of inflammatory pain, postoperative pain, and neuropathic pain Grade III mobilizations of the knee or ankle joint reduce hyperalgesia [27–30,41,42]. Sympathetic excitation also increases in response to mobilization of the cervical spine as measured by an increase in heart rate, respiratory rate, blood pressure, and a changes in skin conductance in human subjects [44].

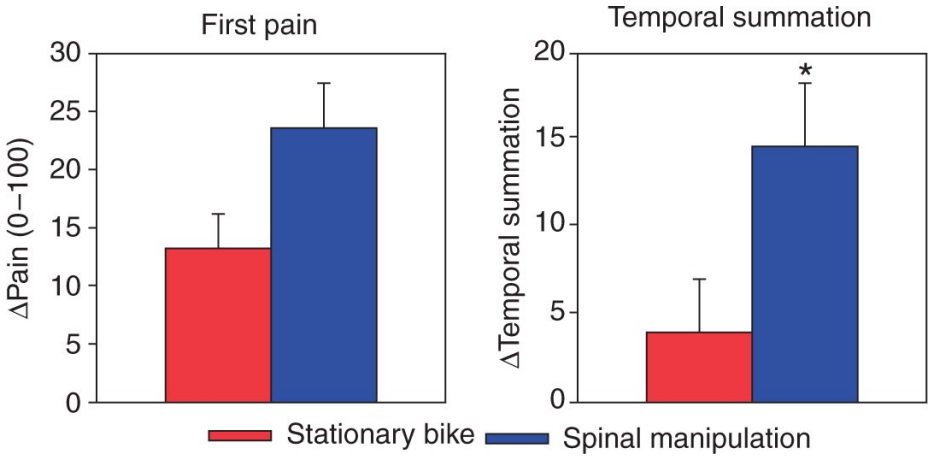

FIGURE 13-1 Spinal manipulation (four thrusts over 5 minutes) was compared with effects of 5-minute of stationary bike on the change in pain to a 47°C heat

stimulus (first pain) and with effects on temporal summation to 47°C heat. A similar increase in pain threshold occurred with both the stationary bike and the spinal manipulation when examining the first pain condition. However, the reduction (Δ) in temporal summation to heat was significantly greater in the group that received temporal summation when compared with the group that used a stationary bike. (Drawn from data presented in George et al. [19].)

The analgesia produced by joint manipulation and mobilization is not reversed by the opioid antagonist naloxone in human subjects [35,46,48] or in an animal model of joint inflammation [41]. However, blockade of peripheral opioid receptors with naloxone prevents the analgesia of joint mobilization in a mouse model of postoperative pain [27]. Using Grade III mobilization of the knee joint in an animal model of ankle inflammation demonstrates that the analgesia produced by such joint mobilization is prevented by spinal blockade of serotonin 5-HT1A and α-2 noradrenergic receptors [41]. However, blockade of GABA or opioid receptors spinally has no effect on the analgesia produced by mobilization [41]. In an animal model of postoperative pain, analgesia produced by ankle joint mobilization is prevented by local or spinal blockade of adenosine A1 receptors [29], systemic blockade of serotonin or yohimbine [29], spinal blockade of cannabinoid-1 receptors [28], and peripheral blockade of cannabinoid-2 receptors [28]. Further in a model of neuropathic pain, joint mobilizations reduce injury-enhanced glial cell activation in the spinal cord, improve impaired motor function, and promote restoration of myelin sheath thickness that is markedly reduced by the nerve injury [30](Fig. 13-2). These data suggest that joint mobilization has effects on both the peripheral and central nervous systems by activating endogenous inhibitory systems and may improve nerve-injury–induced pathology.

Similar to massage, joint mobilizations and manipulations could also produce their effects through improving normal joint range of motion and helping to restore normal movement and muscle recruitment patterns. Mobilization could thus have similar effects on connective tissue morphology through stretching of connective tissue and thus reduce mechanical irritation to peripheral nociceptors reducing input to the central nervous system and thus reduce pain.

CLINICAL EVIDENCE

Several systematic reviews for use of manipulation and mobilization and

massage for the neck and back exist (Table 13-1). These reviews commonly utilize the same literature base to produce their conclusions and have been done as early as 1991. We have used the Cochrane systematic reviews as our primary source for effectiveness and supplement these with subsequent systematic reviews that have highlighted the effectiveness of mobilization and manipulation. One difficulty with randomized controlled trials (RCTs) for manual therapy is the use of an appropriate placebo treatment. Most studies have investigated effectiveness compared with no treatment or to another treatment that might be equally effective, although a few studies have attempted to provide a placebo for mobilization.

Massage/Soft Tissue Mobilizations

Evidence for the use of massage therapy for treatment of painful conditions exists; however, the quality of trials is generally weak, which has made interpretation difficult. Few studies have addressed the appropriate dose in terms of duration of individual visits, number of visits necessary to see an improvement, and frequency of visits. Despite this, massage is commonly utilized to treat musculoskeletal pain conditions and is relatively safe with minimal side effects. This section will describe evidence from systematic reviews and supplement this with additional trials that examine specific issues such as dosing.

In a Cochrane systematic review the effects of massage therapy for low back pain was evaluated compared with sham (N = 2) or other therapies (N = 8): exercise, joint mobilization, relaxation therapy, physical therapy, acupuncture and self-care education, corset, and TENS. They report that massage was superior to sham treatment for pain and function for both short-term and long-term follow-ups, similar to exercise, superior to joint mobilization, relaxation therapy, physical therapy, acupuncture, and self-care education [18]. For individuals with fibromyalgia, a systematic review identified 9 trials with 404 patients and performed a meta-analysis of the data. They show that massage therapy for more than 5 weeks significantly improves pain, anxiety, and depression but not sleep [22]. For mechanical neck pain, a Cochrane review identified 15 trials with low to very low quality. They show that massage may be more effective than control or placebo in improving tenderness and function and may be more beneficial than education. Ischemic compression and passive stretch may be more effective in combination than individually for reduction in pain. Because of the low-quality or lack of reporting of specific techniques used, no recommendations for practice were made but the authors suggest that

massage may provide an immediate short-term effect for pain and tenderness [33]. A Cochrane review examined the effects of transverse friction massage for tendonitis (elbow epicondylitis or lateral knee tendonitis [iliotibial band syndrome]) and found two RCTs with 57 participants meeting the inclusion criteria. In both cases deep friction massage combined with other physical therapy treatments compared with physical therapy treatments alone showed no significant difference between groups [23]. For tension-type headache, soft tissue mobilization and massage techniques showed limited evidence for reduction in pain intensity and frequency [12].

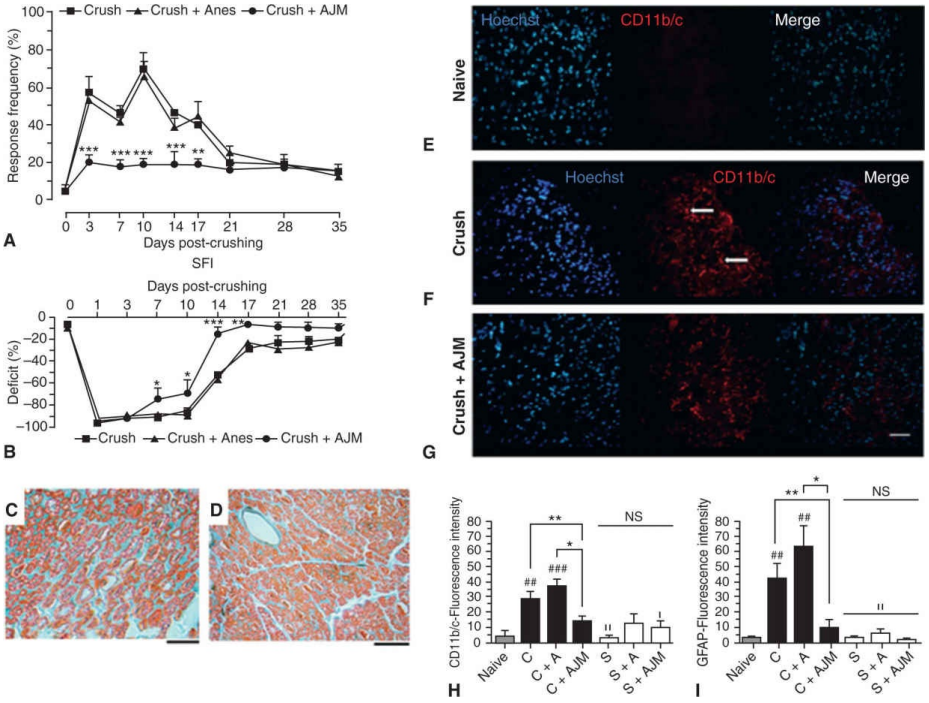

FIGURE 13-2 Using an animal model of neuropathic pain, induced by crushing the sciatic nerve, the effects of ankle joint mobilization (AJM) were examined in nociceptive mechanical hyperalgesia **(A)**, motor function **(B)**, on nerve regeneration **(C, D)**, and spinal glial cell activation **(E–I)**. **A:** The number of responses to repeated stimulation significantly increases after nerve crush. Repeated AJM (every other day for 15 sessions) significantly reduced this enhanced responsiveness to noxious mechanical stimulation. **B:** As a measure of nerve function, animals were assessed using gait analysis (sciatic function index; SFI) and those with AJM show a faster recovery of function. Nerve crush results in histological changes in structure of the nerve with the most prominent feature showing reduced thickness of the myelin sheath **(C)**. AJM showed a significantly greater thickness of the myelin in the sciatic nerve **(D)**. Glial cell activity in the spinal cord was examined using CD11c as a marker of microglia

(*red*, **E–F**; *blue*, nuclear stain). Notice minimal activity of microglia in naïve, uninjured animals. Microglial activity is significantly increased in animals after nerve crush, and repeated AJM significantly reduced the enhanced microglial cell activity induced by nerve crush. **H:** Shows the quantification of CD11c immunoreactivity in the dorsal horn from animals after nerve injury **(C)**, after nerve injury plus anesthesia (C + A), after nerve injury with AJM (C + AJM), and in control groups (naïve, sham [S], S + A, and S + AJM). **I:** Shows quantification for the astrocyte marker GFAP in the same group presented in H. (Reprinted with permission from Martins et al. [30].)

TABLE 13-1 Systematic Reviews for Manual Therapy

References	Condition	Number of Studies	Source	Findings
[18]	Low back pain	$N = 10$	Cochrane database of systematic reviews	Massage better than sham for pain relief and function; similar to other therapies
[22]	Fibromyalgia	$N = 9$	Systematic reviews	Massage improves pain, anxiety, and depression but not sleep
[33]	Neck pain	$N = 15$	Cochrane database of systematic reviews	Massage may be effective for tenderness and function; ischemic compression and passive stretch may be effective for reduction in pain
[12]	Tension-type headache	$N = 1$	Sytematic review	Ineffective for spinal manipulation; limited evidence for soft tissue massage
[23]	Tendonitis of elbow or knee	$N = 2$	Cochrane database of systematic reviews	Deep friction massage combined with other physical therapy treatments not different from physical therapy alone
[7]	Low back pain	N/A	American pain society guidelines	Spinal mobilization/ manipulation effective for acute and chronic low back pain
[20]	Neck pain	$N = 27$	Cochrane database of systematic reviews	Cervical manipulation reduced acute and chronic neck pain; effect was small and may not be clinically effective Thoracic manipulation shows immediate reduction in acute neck pain and increased function
[38]	Acute back pain	$N = 20$	Cochrane database of systematic reviews	Not effective for pain and function
[39]	Chronic back pain	$N = 26$	Cochrane database of systematic reviews	High-quality evidence for spinal manipulation for short-term pain relief and improved function; not more effective than other therapies
[47]	Lateral epicondyalgia	$N = 1$	Systematic review	Mobilization increases pain-free grip and pressure pain thresholds

TABLE 13-1 **Systematic Reviews for Manual Therapy (*continued*)**

References	Condition	Number of Studies	Source	Findings
[4]	Lateral epidondylagia	$N = 1$	Systematic review	Cervical mobilization reduce pain and increase pressure pain thresholds; wrist mobilization similar to other treatments
[24]	Lateral ankle sprain	$N = 3$	Systematic review	Joint mobilization can reduce pain, increases range of motion, and improves function in both acute and chronic sprains
[11]	Musculoskeletal pain	$N = 11$	Systematic review	Limited evidence that neural mobilization reduces pain

A recent clinical trial investigated dosage of massage by varying the duration (30 vs. 60 minutes) and the frequency of the visit (one to three times per week) over 4 weeks against a wait-list control on neck pain. They show that 60-minute treatments two to three times per week significantly reduced pain and dysfunction. No differences over wait-list control occurred with 30 minutes of treatment [40]. Similarly, in people with osteoarthritis, 60 min/w over 8 weeks produced greater reductions in pain and function when compared with 30 minutes [36]. Thus, at least 60 min/session, and one to two times per week appears to produce the greatest reduction in pain and improvement in function.

As practitioners often target their massage through focused soft tissue manipulations, a recent study compared targeted structural massage (focused soft tissue manipulation) to relaxation massage (decrease pain and dysfunction by inducing relaxation) in individuals with nonspecific chronic low back pain. The intervention was 10 treatments over 10 weeks; there were 401 subjects in three groups, active interventions were compared to usual care, and licensed massage therapists provided the treatment. This study showed that both groups showed similar improvements in functional outcomes and symptoms that persisted through 6 months; however, there were no differences between the two types of massage [6].

Cervical Manipulation/Mobilization

For cervical pain, manipulation and mobilization procedures are common clinical procedures aimed at reducing pain and improving function. A Cochrane review of the literature examined the effects of manipulation and mobilization for mechanical neck pain [20]. For the 27 trials selected (1522 participants),

there was low-quality evidence that manipulation and mobilization reduced pain for those with acute or chronic neck pain; yet no difference was observed in function. Moderate evidence that manipulation and mobilization produce similar effects for pain relief is available. The studies show that the effects are small (less than 10 mm on 100-mm pain intensity scale) and may not be clinically significant (generally thought to be greater than 20 mm on 100-mm pain intensity scale). The review found low-quality evidence from two trials (133 participants) that thoracic manipulation provides immediate reduction in acute neck pain and increased function and no added benefit when added to cervical manipulation. This review highlighted that multiple techniques were effective, that effects were immediate or short term, and that the quality of the studies was low. Notably, future studies need to examine for dosing and long-term effects, use larger sample sizes, and examine adverse events.

For lateral epicondylalgia, one systematic review shows that cervical mobilization decreases subjective pain scores and increase pressure pain thresholds [4]. These effects were only studied short term but support the use of cervical mobilization for upper limb pain conditions.

Lumbar Manipulation/Mobilization

Manipulation and mobilization are common treatments for back pain. As such there are several reviews and evidence-based guidelines that have been published. A Cochrane systematic review identified 20 RCTs with 2674 participants. For patients with acute low back pain, spinal manipulative therapy was not more effective for pain and function than control conditions including inert therapy, sham, or comparison group at 1-week, 1-month, 3-to-6-month, or 1-year follow-ups [38]. For chronic low back pain, a Cochrane review included 26 RCTs with 6070 participants, 9 of which had a low risk of bias. This review concluded that there was high-quality evidence for use of spinal manipulation that produced a clinically relevant short-term pain relief and improved function. However, spinal manipulative therapy is not significantly more effective when compared with other therapies, including general practitioner care, analgesics, other physical therapy management, exercises, or back school [39]. Despite these somewhat equivocal findings, evidence-based guidelines developed by the American Pain Society for low back pain recommend the use of manipulation and mobilization for both acute and chronic low back pain [7]. Interestingly, comparison of spinal manipulative therapy, general exercise therapy (strengthening and aerobic exercise), and specific motor control exercises (designed to retrain trunk muscles) in people with low back pain showed

improved short-term effects of spinal manipulation and motor control exercises compared with general exercise therapy, but similar long-term outcomes [14].

Peripheral Joint Mobilization/Manipulation

Whereas most data have examined effects of spinal mobilizations on pain reduction, some studies have investigated the effects of mobilization of peripheral joints. In people with osteoarthritis, a Grade III accessory glide of the tibia increases pressure pain threshold of the knee and the heel and increases function measured by the timed up and go test (TUG) when compared with a placebo treatment or a no treatment control [31]. For people with lateral epicondylalgia, application of Mulligan's mobilization with movement (manual therapy technique with an active movement that is impaired) increases pain-free grip strength and pressure pain thresholds in the treatment group but not in a placebo group or in a no-treatment control groups [34,47]. For people with either acute or chronic ankle sprains a recent systematic review of three articles identified that manual joint mobilization can diminish pain, increase ankle range of motion, and improve function [25].

Neural Mobilization

One systematic review examined the efficacy of neural mobilization for treatment of a variety of musculoskeletal conditions. Of the 11 studies examined the authors concluded that there was limited evidence (Level 3) for the effectiveness of neural mobilization techniques, which included pain reduction [11]. However, all 11 studies utilized different techniques, were single blinded or unblinded, and rated with moderate to low quality.

CONCLUSION

Moderate evidence exists to support the effectiveness of manipulation and mobilization techniques for acute and chronic neck pain, acute and chronic back pain, and lateral epicondylalgia. Limited evidence is available to support the use of massage therapy, soft tissue mobilizations, neural mobilization, and peripheral mobilization and manipulation for treatment of various musculoskeletal pain conditions. The use of peripheral mobilization and soft tissue massage techniques, although common practice for physical therapist, at present has

limited to no evidence to support its use. However, it should be pointed out that there is no negative evidence at present. Clearly future studies need to use appropriate placebo controls and examine a greater proportion of pain conditions.

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SECTION 3

Interdisciplinary Pain Management

CHAPTER 14

Interdisciplinary Pain Management

Harriët Wittink

Chronic pain has been defined as a function of a complex interaction among demographic, physical, psychological, social, and economic factors, including age, sex, education, medical status, pain severity, alcohol and substance abuse, beliefs about pain, increased use of medications and health care services, and a generalized adoption of the sick role [25]. According to the 2011 Institute of Medicine report on relieving pain in America [14], chronic pain affects an estimated 100 million American adults—more than the total affected by heart disease, cancer, and diabetes combined. Chronic pain costs the United States up to $635 billion each year in medical treatment and lost productivity, thus making relieving chronic pain a public health priority.

Because chronic pain is multifactorial in nature, the use of any one modality is bound to fail. John Bonica saw the idea of interdisciplinary collaboration as the key to the understanding of pain and was the first to establish a multidisciplinary pain clinic at the University of Washington in 1960. Many multidisciplinary pain clinics have been developed since then that offer a variety of therapeutic approaches to effective pain management. Marketdata [17] estimated in 2010 that the value of the US market for pain management products and services by clinics, programs, solo anesthesiologists, other MDs, chiropractors, pain drugs, and devices reached $19.6 billion in 2009. Eight percent yearly growth is projected to 2014, to $27 billion. Some of these clinics are modality specific (e.g., nerve block clinics, acupuncture, biofeedback); some are diagnosis specific (e.g., facial pain clinic, pelvic pain clinic); and some are specialized pain centers in which clinicians with expertise in various pain-related disciplines (e.g., physicians, physical therapists, psychologists) work as a team to provide comprehensive pain care.

The Joint Commission developed standards [5] that address the assessment and management of pain in hospitals and other health care settings. The standards acknowledge that patients have a right to effective pain management, and require that the presence of pain be routinely assessed for all patients. The

standards, which have been endorsed by the American Pain Society [8], underscore the importance of effective pain management and establish it as an essential component of quality patient care. The standards apply to ambulatory care facilities, behavioral health care facilities, health care networks, home care, hospitals, long-term care organizations, long-term care pharmacies, and managed behavioral health care organizations. The Commission on Accreditation of Rehabilitation Facilities (CARF) also incorporates principles of the interdisciplinary approach to pain treatment in its pain program accreditation standards [9]. CARF surveys and accredits rehabilitation facilities, including those involved in chronic pain management. Table 14-1 summarizes the most important Joint Commission and CARF standards for pain management.

TABLE 14-1 **Joint Commission and CARF Standards for Pain Management**

Joint Commission Standards	CARF Standards
Recognize the right of patients to appropriate assessment and management of pain	Leadership standards and excellence Pain services are recognized and supported by the facility's executive leaders Leaders at all levels serve as advocates for people with "activity limitations" There is a strategic plan for pain services, and this plan is reviewed and modified regularly
Screen for the existence and assess the nature and intensity of pain in all patients	Rehabilitation process standards* Admission criteria Comprehensive pain assessments are completed at admission and include measures of participant characteristics, physical, psychological, social, financial, and vocational status in addition to pain At admission predicted outcomes are established, as well as a discharge plan Intake information should allow for internal (at the same program over time) and external (other facilities) comparisons
Record the results of the assessment in a way that facilitates regular reassessment and follow-up	Information and outcomes management standards Comprehensive, appropriate, and useful outcomes data must be gathered at admission, discharge, and follow-up using reliable and valid instruments tapping all major outcome domains (e.g., pain, activity, psychosocial, work, etc.) Data must be analyzed regularly and clearly linked to performance improvement activities Programs must compare their actual performance with their expected level of performance and must contrast changes in outcome measures between admission and discharge, and between discharge and follow-up Outcomes must be communicated to stakeholders and to all staff IPR standards Outcomes Programs use outcomes to identify areas for improvement, develop a plan for improvement, implement change, and measure the effects of the change
Determine and ensure staff competency in pain assessment and management, and address pain assessment and management in the orientation of all new staff	Rehabilitation process standards Staff competencies, team functioning Involvement of the consumer in the decision-making process IPR standards† Team composition and function, scope and intensity of treatment, Program Director, Medical Director, Psychologist, and Physician qualifications and responsibilities, staff training Leadership standards Staff are competent in the area of pain services or receive training and supervision in the area according to policies and standards Staffing levels match pain program outcome objectives

TABLE 14-1 **Joint Commission and CARF Standards for Pain Management (*continued*)**

Joint Commission Standards	CARF Standards
Establish policies and procedures that support the appropriate prescription or ordering of effective pain medications	Rehabilitation process standards IPR standards Safety
Educate patients and their families about effective pain management	IPR standards Consumer education, family services
Address patient needs for symptom management in the discharge planning process	Rehabilitation process standards Discharge criteria Comprehensive pain assessments are completed at discharge and include measures of physical, psychological, social, financial, work capability, satisfaction with services, type, duration, and intensity of services provided, and characteristics of the home/transition environment
Maintain a pain control performance improvement plan	Rehabilitation process standards At some point after discharge, follow-up measures of physical, psychological, social, financial, work capability, satisfaction with services, and home environment are conducted from a representative sample of participants The time frame chosen for follow-up should allow for measurement of the durability of the rehabilitation outcomes attained

*Rights of the persons served at the level of the organization, program, and treatment team.

†Interdisciplinary pain rehabilitation.

The International Association for the Study of Pain (IASP) believes that patients throughout the world would benefit from the establishment of a set of desirable characteristics for pain treatment facilities and detailed five different types of pain programs [15]:

1. **Pain treatment facility:** A generic term used to describe all forms of pain treatment facilities without regard to personnel involved or types of patients served. Pain unit is a synonym for pain treatment facility.
2. **Multidisciplinary pain center:** An organization of health care professionals and basic scientists, which includes research, teaching, and patient care related to acute and chronic pain. This is the largest and most complex of the pain treatment facilities and ideally would exist as a component of a medical school or teaching hospital. Clinical programs must be supervised by an appropriately trained and licensed clinical director; a wide array of health care specialists is required, such as physicians, psychologists, nurses, physical therapists, occupational therapists, vocational counselors, social workers, and other specialized health care providers.

The disciplines of health care providers required are a function of the varieties of patients seen and the health care resources of the community. The members of the treatment team must communicate with each other on a regular basis, both about specific patients and about overall development. Health care services in a multidisciplinary pain clinic must be integrated and based upon multidisciplinary assessment and management of the patient. Inpatient and outpatient programs are offered in such a facility (for further details, see appendix at the end of this chapter).

3. **Multidisciplinary pain clinic:** A health care delivery facility staffed by physicians of different specialties and other nonphysician health care providers who specialize in the diagnosis and management of patients with chronic pain. This type of facility differs from a multidisciplinary pain center only because it does not include research and teaching activities in its regular programs. A multidisciplinary pain clinic may have diagnostic and treatment facilities, which are outpatient, inpatient, or both.
4. **Pain clinic:** A health care delivery facility focusing upon the diagnosis and management of patients with chronic pain. A pain clinic may specialize in specific diagnoses or in pains related to a specific region of the body. A pain clinic may be large or small but it should never be a label for an isolated solo practitioner. A complex health care institution that offers appropriate consultative and therapeutic services with a single physician could qualify as a pain clinic, if chronic pain patients were suitably assessed and managed. The absence of interdisciplinary assessment and management distinguishes this type of facility from a multidisciplinary pain center or clinic. Pain clinics can, and should be encouraged to, carry out research, but it is not a required characteristic of this type of facility.
5. **Modality-oriented clinic:** This is a health care facility that offers a specific type of treatment and does not provide comprehensive assessment or management. Examples include nerve block clinic, acupuncture clinic, biofeedback clinic, etc. Such a facility may have one or more health care providers with different professional training; because of its limited treatment options and the lack of an integrated, comprehensive approach, it does not qualify for the term multidisciplinary.

Although the IASP taskforce that put together the set of desirable

characteristics for pain treatment facilities does not differentiate between multidisciplinary and interdisciplinary treatment, there is a difference. Fordyce et al. [11] wrote:

> "In a multidisciplinary exercise, two or more professions may make their respective contributions, but each contribution stands on its own and could emerge without the input of the other. In an interdisciplinary effort, life is not so simple. The end product requires that there be an interactive and symbiotic interplay of the contributions from different disciplines. Without that interaction, the outcome will fall short of the need. The essence of the matter is that each of the participating professions needs the others to accomplish what, collectively, they have agreed are their objectives."

Multidisciplinary treatment is a treatment in which multiple providers from different disciplines contribute to care. Interdisciplinary treatment is treatment provided by multiple providers from different disciplines that integrate care as a team, through frequent communication and common goals.

In this chapter interdisciplinary pain management and the evidence for interdisciplinary pain management will be further discussed.

INTERDISCIPLINARY PAIN MANAGEMENT

The biopsychosocial approach to pain and disability is widely accepted as the most heuristic perspective to the understanding and treatment of chronic pain disorders and has replaced the outdated biomedical reductionistic approach. The biopsychosocial approach views pain and disability as a complex and dynamic interaction among physiologic, psychologic, and social factors that perpetuates —and may even worsen—the clinical presentation [13]. The Institute of Medicine report, *Relieving Pain in America* [14], reinforced the importance of framing chronic pain as a unique chronic disease state with complex neurophysiological, emotional, and social components—all of which make its management quite distinct from that of acute pain. The "suffering" aspects of chronic pain require a different level of attention and intervention than that available through medications alone. Traumatic experiences, depression, changes in self-image, disruptions in employment and other social roles, stresses on family caregivers, and a host of other subtle aspects of chronic pain clearly point

to the need for a biopsychosocial treatment model. Cognitive behavioral therapies and the development of coping skills have demonstrated effectiveness in pain management, and patients' motivation and engagement are important in establishing realistic goals for the management of their pain. A collaborative model of care is thus critically important to a successful outcome. As chronic pain affects multiple domains of life, patients with chronic pain therefore require multidimensional assessment and treatment, which is best done by an interdisciplinary team.

CARF has defined interdisciplinary pain rehabilitation programs as interdisciplinary pain management in comprehensive pain programs involves health care providers from several disciplines, each of whom specializes in different features of the pain experience.

> "outcomes-focused, coordinated, goal-oriented interdisciplinary team services. The program can benefit persons who have impairments associated with pain that impact their activity and participation. An Interdisciplinary Pain Rehabilitation Program measures and improves the functioning of persons with pain and encourages their appropriate use of healthcare systems and services."

In the interdisciplinary management of chronic pain, the core team typically comprises a pain management physician, a psychologist, a nurse specialist, a physical and occupational therapist, a vocational counselor, and a pharmacist, although owing to poor reimbursement issues, many interdisciplinary teams have had to scale back in personnel. CARF requires that all accredited programs have a board-certified medical director and a psychologist on staff. The various disciplines have different roles within the team (Table 14-2), which may overlap, predominantly between behavioral approaches to the patient by the psychologist and occupational and physical therapists. This overlap helps to reinforce the same message to the patient by the various care providers.

The initial screening of the patient by a member of the core team determines which members of the team will be needed for a complete assessment of the patient. The assessment should include all major outcome domains: pain, physical, psychological, social, and vocational functioning, using reliable and valid instruments that preferably are sensitive to change.

After this evaluation, the entire core team discusses about the patient and a comprehensive treatment plan is developed. The care team tailors the care plan according to the individual needs of the patient, with a focus on achieving measurable treatment goals established with the patient. Therapeutic goals for

multidisciplinary pain programs (MPPs) are generally multifaceted. Among the most common are goals aimed to:

- Reduce pain;
- Improve function;
- Permit return to work;
- Resolve medication issues; and
- Reduce health care utilization [20].

TABLE 14-2 Roles of the Members of the Interdisciplinary Pain Management Team

Physician	Comprehensive assessment patient, review of prior records and previous treatments. Consideration of medical, block, or implantation interventions
Psychologist	Comprehensive psychological assessment, focus on coping mechanisms and presence of psychological illness and/or psychiatric comorbidities, substance abuse potential Development of psychological interventions, including education on the use of self-management techniques, education, and cognitive-behavioral therapy
Nurse	Coordination of care, education, medical therapy
Physical therapist	Comprehensive assessment, with emphasis on the musculoskeletal system, assessment of strength, flexibility, and physical endurance. Assessment of functional activities and behavior. Education on pain pathophysiology, active physical coping skills, management of physical rehabilitation process
Occupational therapist	Assessment of the work site and home. Assessment of need for adaptive equipment. Setting functional goals. Education on active coping skills, assertiveness training, relaxation and distraction techniques
Vocational rehabilitation	Assess vocational skills and identify opportunities and strategies to return to work
Pharmacist	Comprehensive review of past and current pharmacological interventions including the use of herbal and homeopathic substances, education of patient with regard to appropriate use of pharmacological interventions
Psychiatrist	Diagnosis and treatment of psychiatric comorbidities Medication management of psychiatric problems

Source: Adapted from Ashburn and Staats [2].

The plan must fit the patient's abilities and expectations. For some individuals, education and medical management suffice, whereas for others care may need to include an inpatient pain program that requires the patient to remain at a treatment center 24 hours a day, 7 days a week, for 3–4 weeks, or an outpatient pain rehabilitation program that can vary according to the facility from 8 hours a day, 5 days a week for 2–4 weeks, to 2 hours a day, 3 days a week for 6–8 weeks. Negotiating the overall treatment plan is the collective responsibility of the team and the patient.

Contingencies for possible outcomes should also be agreed on by the team and patient. Agreements should be clear and are best placed in writing. Contracts are a simple and effective means of avoiding future confusion about the plan. Written contracts offer the patient the opportunity to review and consider the information over time.

Team unity is critical to managing any patient, but especially to the difficult patient. Unity is largely a function of communication and understanding and respecting the expertise of the other team members. Frequent team meetings connect key representatives of the treatment team. Patient progress should be discussed during the meetings. If patients are not meeting their goals, are inconsistent with their attendance, or do not follow through with recommendations, the team should make recommendations for continuation of therapy or discharge. Because it might be impossible to meet with the entire team, there should be a mechanism for disseminating the plan between clinicians. Preferentially, the plan is put in writing, as doing so documents both the interdisciplinary effort of the team and provides a sequence of events during the treatment of a patient. Frequent reassessment can help determine if the patient progresses according to plan and whether the patient can be discharged with their goals met. At discharge a follow-up plan should be made with the patient and comprehensive pain assessments completed that include measures of physical, psychological, social, financial, work capability, satisfaction with services, type, duration, and intensity of services provided, and characteristics of the home/transition environment.

WHERE WE ARE NOW?

In a survey of the treatment of chronic pain [17], a worrying trend was noted. In 2010, the field was composed of 3900 anesthesiologists, another 4000–5000 other MDs (general practitioners, family doctors, physiatrists) who give injections, 366 accredited pain programs/clinics (mostly hospital or university-based), and 700+ pill mills. More anesthesiologists continue to enter the field, with 3900 now active in pain therapy. To date, 4100 anesthesiologists have been certified in pain therapy. “The field has degenerated into turmoil as accredited multidisciplinary programs compete with solo anesthesiologists, illegal ‘pill mills’ selling Oxycontin, and other MDs providing injections after taking a weekend course. Profits, not patient care and effective outcomes, are the focus. And, a majority of consumers don’t know how to find legitimate pain

management practitioners." This change in pain management health care seems most likely because of reimbursement issues.

Multidisciplinary programs use a large number of staff and have an average price tag of $12,000–$15,000, which limits the number of clients that can afford it [17]. In the United States, the number of programs has been greatly reduced in the last decade as a result of reduced reimbursement. As of 2005, there were 84 pain programs in the United States accredited by CARF as interdisciplinary pain rehabilitation programs [24]. A 2010 search on the CARF website yielded just 64 programs and a 2015 search yielded 89 accredited outpatient and 3 inpatient programs in the United States. On the other hand, in other developed nations, the availability of interdisciplinary chronic pain care appears to be increasing dramatically, with Canada having the lowest number of citizens (172.413) per clinic [4]. In 2010, a group of pain experts from 15 European nations produced a consensus report on the management of chronic pain that highlighted the need for multidisciplinary approaches [3].

In the 2011 Agency for Healthcare Research and Quality (AHRQ) technical brief on MPPs for chronic non-cancer pain [16], the authors defined MPP as providing interdisciplinary care: providers from each of the components work together to develop the treatment plan. AHRQ, found over 180 papers, representing approximately 160 different experiments or observational trials.

These studies were based in 18 different countries. Approximately half of the papers included (96) were located in the United States. The majority of the remainder was conducted in Europe/the United Kingdom (68). Around half the studies (90 out of 183) included multiple pain conditions. The remaining 93 studies focused on a single condition, 85% of these on back pain. This overview of the literature on MPPs suggests that a majority of the studies had no comparison population. In addition, the continuity or persistence of treatment effects was difficult to estimate based on existing studies because of large numbers of participants lost to follow-up and attrition. For a discussion on "where to go from here" please see the Next Steps section of the AHRQ report. A number of systematic reviews have attempted to elucidate the effectiveness of interdisciplinary pain programs of which we provide a summary below.

EFFECTIVENESS OF INTERDISCIPLINARY PAIN TREATMENT

There is considerable evidence for the effectiveness of multidisciplinary

treatment programs for low back pain. Several systematic reviews have been undertaken to evaluate their effectiveness. However, it should be noted that most clinical trials have been done without comparison with a control intervention. Most have been compared with waiting lists and some have been directly compared with standard care. In a systematic review on the effectiveness of physical and rehabilitation interventions for chronic nonspecific low back pain, van Middelkoop et al. [29] found moderate evidence for the effectiveness of a multidisciplinary treatment compared with no treatment and other active treatments at reducing pain at short term in the treatment of chronic low back pain. Gatchel and Okifuji [13] conducted a comprehensive review of all studies in the scientific literature reporting treatment outcomes for patients with chronic pain. They found that MPPs result in varying degrees of pain reduction, from 14–60% to an average of 20–30%. These figures are comparable to the most conventional medical management of chronic pain with opioids, which yield an average pain reduction of 30%. Approximately a 65% increase in physical activity is observed following MPP treatments. In contrast, only a 35% increase is reported in patients receiving conventional medical care. Return to work rates following MPP range from 29% to 86%, with a mean of 66%, whereas conventional medical treatments consistently yielded lower rates, from 0% to 42%, with a mean rate of 27%. Health care utilization data from MPP trials generally yield favorable results, with reduced additional therapy for pain seeking within 1 year following the treatment, reductions in the subsequent hospitalization, surgical intervention, and medication use.

A systematic review on functional restoration programs for low back pain found that most published studies reports favorable return-to-work rates at 1 and 2 years (from 65% to 90%) after functional restoration programs. Social security systems probably play a pivotal role in outcomes, and data may not be extrapolated from one country to another. Finally, work-hardening programs, when associated with functional restoration programs, probably increase the rate of return-to-work and decrease the number and length of sick leave [21].

In a systematic review of studies comparing comprehensive chronic pain programs with unimodal treatment or no-treatment control patients, which involved a total of 3089 participants, McCracken and Turk [18] reported the following outcome comparisons: return to work, 68% CPP versus 32% unimodal or no treatment; pain reduction, 37% versus 4%; medication reduction, 63% versus 21%; and increases in activity, 53% versus 13%, respectively.

Gatchel and Okifuji [13] conducted a comprehensive review of all studies in the scientific literature reporting treatment outcomes for patients with chronic pain. They found that MPPs result in varying degrees of pain reduction, from

14% to 60% with an average of 20–30%. These figures are comparable to the most conventional medical management of chronic pain with opioids, which yield an average pain reduction of 30%. Approximately a 65% increase in physical activity is observed following MPP treatments. In contrast, only a 35% increase is reported in patients receiving conventional medical care. Return-to-work rates following MPP range from 29% to 86%, with a mean of 66%, whereas conventional medical treatments consistently yielded lower rates, from 0% to 42%, with a mean rate of 27%. Health care utilization data from MPP trials generally yield favorable results, with reduced additional therapy for pain seeking within 1 year following the treatment, reductions in the subsequent hospitalization, surgical intervention, and medication use.

Similarly, a meta-analysis of studies evaluating chronic pain treatment programs found that, in comparison with no treatment and single-modality methods, patients participating in interdisciplinary programs demonstrated long-term improvement [10]. Chronic pain patients in this type of treatment functioned better than 75% of control patients. They had significant improvements regarding activity level, pain intensity, pain behaviors, and use of medication and health services compared with the no-treatment group. In addition, 68% of the patients returned to work, versus 36% of the untreated patients.

Interestingly, patients who did not have physical therapy treatment (because of reimbursement issues) exhibited significantly worse functioning and a lower percentage who were working, relative to those who did have physical therapy treatment; these gains were maintained for long term. These findings suggest that patients who did not receive physical therapy treatment did not experience the same benefits of interdisciplinary pain management as the subjects who received all of their treatment in the same clinic.

In summary, there is moderate evidence that interdisciplinary care programs reduced pain and improved function. Physical therapy is a critical factor in functional improvement in interdisciplinary programs. In particular, these programs have the greatest effect on functional measures, return to work, and health care utilization, especially when physical therapy is included in the interdisciplinary program. A German systematic review on cost-effectiveness of MPPs in the treatment of chronic low back pain (CLBP) found three articles that demonstrated moderate to high cost-effectiveness [23]. Another systematic review on patients with chronic pain found that MPPs provide comparable reduction in pain to alternative pain treatment modalities, but with significantly better outcomes for medication use, health care utilization, functional activities, return to work, closure of disability claims, and with substantially fewer

iatrogenic consequences and adverse events. MPPs were significantly more cost effective than implantation of spinal cord stimulators, implantable drug delivery systems, conservative care, and surgery, even for selected patients [26]. Another review comparing MPPs with conventional medical treatments found that MPPs offer the most efficacious and cost-effective treatment for persons with chronic pain [13]. In a Swedish randomized controlled multicenter trial, 214 patients with chronic pain were randomized to one of three (physical therapy, cognitive behavioral therapy, or vocational multidisciplinary rehabilitation) active treatment conditions or to a control group receiving treatment-as-usual. A 10-year follow-up study found that the vocational multidisciplinary program was most successful in reducing sick days (43 days compared with physical therapy 17 days and cognitive behavioral therapy 13 days). The effects were most pronounced in the first 3 years after rehabilitation [7].

PREDICTORS OF OUTCOME IN INTERDISCIPLINARY PAIN PROGRAMS

In a recent systematic review on influence of dose on outcome of MPPs, 18 randomized controlled trials (RCTs) were included. Analyses showed that evaluation moment, number of disciplines, type of intervention, duration of intervention in weeks, percentage of women, and age influenced the outcomes of MPPs. The independent effect of dose variables could not be distinguished from content because these variables were strongly associated [30].

Van der Hulst et al. [28] studied predictors of outcome of multidisciplinary rehabilitation or back-school treatment for patients with chronic low back pain. Outcome was measured as activity limitation or participation restriction. It was impossible to define a generic set of predictors of outcome of multidisciplinary rehabilitation and back schools for patients with chronic low back pain because the reviewed studies were descriptive or exploratory in nature, and most predictors were only studied once. Nevertheless, for several predictors, consistent evidence was found. Patients with high pain intensity and/or problems at work (e.g., functioning at work, dissatisfaction) were likely to have poor treatment outcome. In contrast, the low use of active coping skills and high perceived limitations of activity at baseline may predict better treatment outcome.

As a group, in comparison with clinical trials in other areas of therapy, RCTs related to pain tend to be of low quality because of the small numbers of patients

enrolled; flaws in patient randomization, assignment, and retention; scanty descriptions of the patients enrolled; and heterogeneity in the methods and timing of assessment of pain and other outcomes [31]. Many interventions in pain control RCTs are sparse and too disparate to consolidate [1]. Thus, for much of clinical practice there is still no "best evidence." The studies cited above seem to indicate that interdisciplinary pain management helps our patients. Patients with chronic pain are not a homogeneous group and different interventions may be indicated for different subgroups of patients [27]. Matching treatment to patient characteristics has been shown to improve outcomes of clinical care [6]. We still have a long way to go, however, in determining which patients benefit from which treatments, but we need to solve this in interdisciplinary teams.

WHY INTERDISCIPLINARY TREATMENT IS NOT THE RECOGNIZED STANDARD OF CARE

Meldrum [19] identified three dichotomies that have held the MPPs back from being the "recognized standard of care in the United States": (1) disciplinary collaboration in MPPs versus the "discipline-segmented organization of major medical centers," (2) collaborative care in MPPs versus the fee-for-service model of health care payments, and (3) rehabilitative treatment in MPPs "focused on individualized assessment and patient behavior change" versus the curative medical model of treatment. A fourth problem is that instead of authorizing full multidisciplinary pain management programs, health insurance carriers have been "carving out" portions of comprehensive, integrated programs (i.e., sending patients to different providers for their various needs outside of the comprehensive pain management programs), thus diluting the proven successful outcomes of such integrated programs in an effort to cut cost [12,16]. For instance; Robbins et al. [22] showed that patients who completed interdisciplinary pain management demonstrated significant improvements on the majority of outcome measures, and maintained these gains at 1-year follow-up, relative to treatment dropouts. This was true for measures of both physical and psychosocial functioning, suggesting that the treatment program had a significant effect on all aspects of the experience of chronic pain. Furthermore, treatment completers showed significant positive changes in work status from pretreatment to posttreatment, with only 14.6% not working because of the original injury at posttreatment, and these gains were maintained at 1-year follow-up, again revealing that interdisciplinary pain management had a lasting

positive effect on vocational status. Meldrum's first dichotomy draws attention to the requirement in an MPP of significant integration of care across several disciplines; major medical centers are aligned in silos by field and are increasingly competitive with each other for resources, including patients, floor plan, and research dollars. The second dichotomy points to the difficulty MPPs have getting adequate reimbursement for the time-intensive assessments and collaborative meetings needed to provide intensive multidisciplinary treatment. Meldrum's third dichotomy is driven not just by health care payers and providers, but also by patients themselves. It is perhaps inevitable that a person in pain would seek a surgical cure or a pill over the intensive cognitive and behavioral changes required by an MPP [16].

WHAT TO DO WHEN YOU CANNOT "GO INTERDISCIPLINARY"

Most physical therapy interventions for patients with chronic pain are unidisciplinary, meaning care is not integrated with other health care providers. It is helpful to form unofficial alliances with the patient's various care providers. Although time consuming, it is necessary, as it prevents misunderstandings between care providers and the patient getting conflicting information from providers. Physical therapists must work with pain psychologists for optimal treatment of patients. Patients with chronic pain have high rates of concurrent anxiety and depression, and some may have suicidal ideation. Many have diagnosed (some undiagnosed) psychiatric illnesses or personality disorders, or both. Addressing psychological problems is not only far beyond the scope of physical therapy practice, it is also irresponsible. Referral to psychologists specialized in the treatment of patients with chronic pain is discussed in Chapter 10.

APPENDIX: DESIRABLE CHARACTERISTICS OF MULTIDISCIPLINARY PAIN CENTERS

The following are the desirable characteristics of multidisciplinary pain centers [15]:

1. A multidisciplinary pain center (MPC) should have on its staff a variety

of health care providers capable of assessing and treating physical, psychosocial, medical, vocational, and social aspects of chronic pain. These can include physicians, nurses, psychologists, physical therapists, occupational therapists, vocational counselors, social workers, and any other type of health care professional who can make a contribution to patient diagnosis or treatment.

2. At least three medical specialties should be represented on the staff of an MPC. If one of the physicians is not a psychiatrist, physicians from two specialties and a clinical psychologist are the minimum required. An MPC must be able to assess and treat both the physical and the psychosocial aspects of a patient's complaints. The need for other types of health care providers should be determined on the basis of the population served by the MPC.
3. The health care professionals should communicate with each other on a regular basis both about individual patients and the programs that are offered in the pain treatment facility.
4. There should be a Director or Coordinator of the MPC. He or she needs not be a physician, but if not, there should be a Director of Medical Services who will be responsible for monitoring of the medical services provided.
5. The MPC should offer diagnostic and therapeutic services, which include medication management, referral for appropriate medical consultation, review of prior medical records and diagnostic tests, physical examination, psychological assessment and treatment, physical therapy, vocational assessment and counseling, and other facilities as appropriate.
6. The MPC should have a designated space for its activities. The MPC should include facilities for inpatient services and outpatient services.
7. The MPC should maintain records on its patients so as to be able to assess individual treatment outcomes and to evaluate overall program effectiveness.
8. The MPC should have adequate support staff to carry out its activities.
9. Health care providers active in an MPC should have appropriate knowledge of both the basic sciences and clinical practices relevant to chronic pain patients.
10. The MPC should have a medically trained professional available to deal with patient referrals and emergencies.
11. All health care providers in an MPC should be appropriately licensed in the country or state in which they practice.

12. The MPC should be able to deal with a wide variety of chronic pain patients, including those with pain due to cancer and pain due to other diseases.
13. An MPC should establish protocols for patient management and assess their efficacy periodically.
14. An MPC should see an adequate number and variety of patients for its professional staff to maintain their skills in diagnosis and treatment.
15. Members of an MPC should be carrying out research on chronic pain. This does not mean that everyone should be doing both research and patient care. Some will only function in one arena, but the institution should have ongoing research activities.
16. The MPC should be active in educational programs for a wide variety of health care providers, including undergraduate, graduate, and postdoctoral levels.
17. The MPC should be part of or closely affiliated with a major health sciences educational or research institution.

Desirable Characteristics for a Multidisciplinary Pain Clinic

The distinction between an MPC and a multidisciplinary pain clinic is that the former has research and teaching components that need not be present in the latter. Hence, items 15, 16, and 17 mentioned above are not required for a multidisciplinary pain clinic. All of the other items should be present.

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CHAPTER 15

Medical Management of Pain

Eva Kosek

Pain can be conceptualized as a primarily motivational state to induce a behavioral drive with the purpose to restore homeostasis. Acute pain can be regarded as an important warning signal, which is supported by the severe tissue injuries sustained by people with an inherited inability to feel pain. The intensity of acute pain is generally proportional to the extent of injury (i.e., nociceptive input), but that is not necessarily true for chronic pain. On the contrary, the intensity of chronic pain often correlates poorly with the degree of peripheral pathology, as in osteoarthritis [75] and rheumatoid arthritis [93]. Pain can even persist without any identifiable organic pathology, as in fibromyalgia [21]. The perception of pain can be described in terms of sensory-discriminative, affective, and cognitive dimensions [74].

Imaging studies assessing pain-related cerebral activation support the multidimensionality of the pain experience. These studies have documented activation of brain areas traditionally associated with the perception of sensory features, as well as regions associated with emotional and motivational aspects of pain during evoked pain in healthy individuals [22]. In chronic pain patients, activation of the somatosensory cortex was only seen during brief periods of spontaneously increasing pain intensity. During periods of stable ongoing pain, only brain regions of importance for emotional and cognitive aspects of pain (the prefrontal and cingulate cortices) were activated [11]. Furthermore, the processing of clinical pain changed over time from sensory (similar to processing acute/evoked pain) to more emotional/cognitive activation patterns (mainly prefrontal cortex, cingulum, and amygdala) [44]. These studies indicate a greater emotional salience of chronic pain compared with experimental pain and stress the importance of coping strategies influencing the perception of chronic pain. Finally, overlapping functional and structural brain changes, with reduced brain volumes, have been reported in chronic pain patients [49]. Chronic pain should therefore be regarded not solely as a symptom, but as a medical problem in itself.

CLINICAL ASSESSMENT OF THE PATIENT WITH PAIN

The medical assessment of a person with pain always includes a careful history and physical examination. Depending on the results, the physician must decide whether additional laboratory tests or radiological or neurophysiological examinations are needed in order to define the diagnosis and to exclude potentially dangerous and treatable medical conditions. The physician must always consider whether the cause of pain can be treated. For example, surgery may be appropriate in patients with severe pain due to osteoarthritis, or disease-modifying treatments may be helpful in patients with rheumatoid arthritis. Unfortunately, causal treatment is not always possible.

The next step is to consider treatments that can relieve the pain (i.e., symptomatic treatment), such as physiotherapy or pharmacotherapy. Despite these interventions, many patients are still left with chronic pain that affect their function and quality of life in a negative way. Chronic pain can severely affect psychological well-being, cognitive functions, and physical activity. To make a complete assessment of a chronic pain patient, all dimensions of pain (sensory, affective, cognitive, and motor) must be analyzed in addition to the social context (the patient's ability to function as a spouse, parent, or employee). Interventions to help patients to cope better with their pain and to reduce the negative effects of pain on daily life should be considered. Cognitive-behavioral therapy (see Chapter 13) and multiprofessional team-based rehabilitation programs (see Chapter 11) have proven effective in this regard.

History

A careful history in combination with a pain drawing is usually sufficient to give a good working hypothesis as to the nature of the pain problem and provide guidance for further investigations. The history should include heredity of interest, past and present disease, previous investigations, and previous treatments and their results. The patient should be asked to fill in a pain drawing, mapping the location of pain and other symptoms such as numbness and paresthesias. Ratings of the present, minimal, and maximal pain intensity should be gathered. The duration of pain, diurnal variation in pain intensity, as well as pain-aggravating factors (such as movements or stress) and pain-relieving factors need to be assessed. The history should also include psychosocial factors

of relevance (especially in chronic pain patients) such as depression, anxiety, anger, coping strategies, cognitive difficulties, sleep disturbance, and the patient's perception of stress, problems with relationships, and function (including work capacity).

Physical Examination

All patients should be examined with the goal of identifying the cause of pain. In nonsevere acute pain conditions, the examination can usually be restricted to the painful part of the body, whereas patients with long-term or severe pain need a more extensive examination. Neurological evaluation (including sensitivity testing, reflexes, and exclusion of paresis and fasciculation), relevant examination of the musculoskeletal system (examination of joints and muscles, including functional measures), and a psychological assessment (assessment of depression and anxiety) usually form part of the examination. Additional investigations that may be required for certain patients include laboratory tests, radiological examinations, neurophysiological examinations—quantitative sensory testing (QST), electroneurography, and electromyography—and/or referral to other specialists for further investigation and treatment. Given that the diagnosis of neuropathic pain relies heavily on the presence of sensory dysfunction, the examination of sensitivity is of great importance. A complete bedside examination includes assessment of different modalities, such as vibration (tuning fork; Aβ fibers), light touch (brush: Aβ fibers), pinprick (needle; Aδ/C fibers), cold (metal; Aδ fibers), and warmth (heated metal; C fibers). The examination should be guided by the suspected diagnosis. In certain cases, complementary examinations using more sophisticated methods such as QST can be required [43]. Dysfunction of small fibers (Aδ and C fibers) cannot be detected by electroneurography, and thus electroneurography can never replace bedside sensory testing (or QST).

The clinical assessment should result in the definition of the type or types of pain (i.e., nociceptive pain, neuropathic pain, or pain of unknown origin) and a pain diagnosis according to the ICD-10 classification criteria [101]. It is important to acknowledge that one diagnostic entity can give rise to several different pain types, which can be illustrated by lumbar disk herniations, which commonly cause nociceptive pain in the back and neuropathic pain in the leg. The dominant type of pain in a patient with lumbar disk herniation will guide the physician to choose the correct treatment. Accordingly, the same type of pain can occur across various diagnostic entities; for example, nociceptive pain is seen in patients with acute fractures, osteoarthritis, rheumatoid arthritis, and

ischemic ulcers, conditions that clearly demand different medical treatments.

Multidimensional Pain Analysis

In the complex, subjective experience of pain, the sensory, emotional, cognitive, and motor dimensions are constantly interacting. In patients presenting with severe or long-term pain, the role of a multidimensional pain analysis is to assess all of these dimensions in order to obtain a specific profile, which is used for the choice of further treatment (see Fig. 15-1). It is well known that depression [1,31], pain-related anxiety or fear [9,12], kinesiophobia or movement avoidance [8,100], and catastrophizing [91] are strong negative predictors for good treatment outcomes in chronic pain patients. On the other hand, acceptance has been identified as a predictor for good treatment outcomes [70–72]. The beneficial effects of cognitive-behavioral therapy in chronic pain patients are most likely explained by the reduction of negative psychological factors in combination with improved coping skills, increased acceptance, and better self-efficacy [47,97] (see Chapter 13).

The multidimensional pain analysis is best performed as a multiprofessional, team-based assessment, resting on the biopsychosocial pain model. In addition to the sensory aspects (the intensity, localization, and type of pain), emotional and cognitive aspects must be examined (see Chapter 11). Anxiety, depression, pain-related anger, coping strategies, fear-avoidance, and degree of acceptance are assessed during an interview with the patient. Self-administered, standardized questionnaires can be used as a complement to the interview and are also valuable for the assessment of treatment outcome.

Pain can also have negative effects on physical function. Inactivity due to movement-related pain is common in chronic pain patients and leads to decreased muscle strength, reduced endurance, and decreased aerobic capacity. An adequate training regimen can often improve physical capacity and even reduce pain. Nonfunctional body postures, selectively increased muscle tension, problems with coordination, and co-activation of antagonists can develop as a consequence of pain and can be treated by a physical therapist. Fear of movement constitutes a special problem leading to avoidance of certain physical activities. In analogy to treatment of phobias, the treatment consists of a gradual exposure to the physical activity that the patient fears and avoids [100]. Patients with a complex pain profile, involving severe pain along with depression or anxiety, inadequate coping strategies, and fear-avoidance, should be considered for multiprofessional team-based pain treatment and rehabilitation programs.

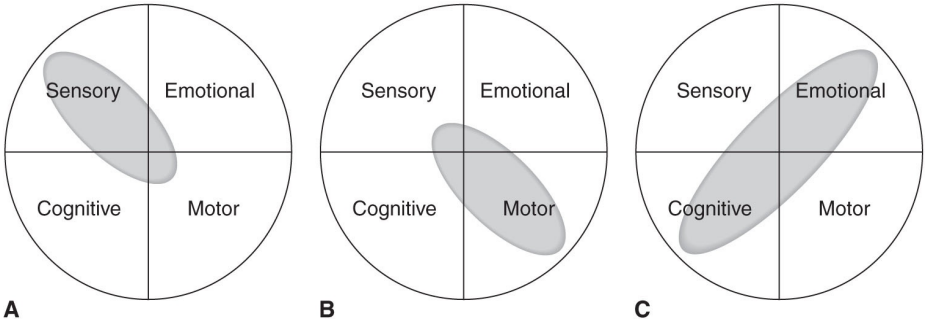

FIGURE 15-1 Multidimensional pain analysis of chronic pain patients and its implication for treatment. **A:** The pain profile of a 67-year-old female patient with nociceptive pain due to osteoarthritis of the hip. She has no psychological symptoms, has good coping strategies, and has remained physically active. This patient was helped by transdermal buprenorphine, which reduced her pain at rest, lessened her sleep disturbance, and improved her quality of life. **B:** The pain profile of a 46-year-old male after surgery for lumbar disk herniation. He was totally relieved of his radicular pain, and his lumbar pain was tolerable. He had no psychological or cognitive complications. However, he was hesitant to resume normal physical activity and had a low functional capacity. This patient improved his function following physical therapy (a graded training regime). **C:** The pain profile of a 52-year-old female patient 2 years after a whiplash trauma. She had developed depression and pain-related anxiety. Her coping method was dominated by catastrophizing and avoidance. She was convinced that because physical activity increased her pain it was harmful to her neck. This patient participated in a multimodal, team-based rehabilitation program including cognitive-behavioral therapy, social counseling, and physical therapy. Despite residual pain, she improved her function and returned to work (half-time).

When Should a Physical Therapist Refer to a Pain Specialist?

The physical therapist should refer a patient to a pain physician if one or more of the following situations is present: (1) lack of a pain diagnosis, or symptoms that are not in accordance with the analysis made; (2) lack of positive treatment effect of physical therapy despite adequate compliance and duration of treatment; (3) worsening of pain or presentation of new symptoms requiring investigation; (4) inadequate pain treatment (i.e., need for pharmacotherapy or other forms of pain relief that cannot be provided by the physical therapist); (5) “red flags” such as weight loss, severe fatigue, initial pain onset at 55 years or older, recent trauma, pain that worsens at night, a history of cancer, steroid consumption, very poor general health, severe disability, or sleep disorder, any

sign of systemic disease such as infection, inflammatory disorder, neurological disorder (unless accounted for and adequately treated), or any suspicion of a previously unrecognized medical condition; (6) suspicion of overconsumption of analgesics, drug abuse, or alcohol abuse; (7) psychological symptoms that need additional treatment (depression, anxiety, or catastrophizing); (8) a complex pain profile indicating that patients are likely to need treatment by a multiprofessional team.

DIFFERENT TYPES OF PAIN

According to the current IASP terminology, two types of pain are currently acknowledged, that is, nociceptive and neuropathic pain. In addition, the term "pain of unknown origin" (idiopathic pain) is often used in clinical praxis. The correct identification of pain type is clinically important because each type of pain requires a different treatment strategy.

Nociceptive Pain

IASP defines nociceptive pain as "pain that arises from actual or threatened damage to non-neural tissue and is due to activation of nociceptors." The term is used to describe pain "occurring with a normally functioning somatosensory nervous system to contrast with the abnormal function seen in neuropathic pain." The intensity of acute nociceptive pain is usually proportional to the degree of injury or tissue pathology and responds well to antinociceptive pharmacotherapy. In cases of long-term nociceptive pain, changes in the function of endogenous pain modulatory mechanisms (i.e., central hyperexcitability including disinhibition) are commonly seen. There are currently no acknowledged diagnostic criteria to detect central hyperexcitability, but increased pain intensity, spread of pain to previously unaffected parts of the body, and increased sensitivity to stimulus-evoked pain in the absence of corresponding aggravation of the peripheral pathology are considered characteristic. The distinction between nociceptive pain with profound central hyperexcitability and pain where the central hyperexcitability is believed to be the dominating pain generator (sometimes referred to as dysfunctional pain) is difficult, and there are currently no acknowledged guidelines for the clinician to use. However, this distinction is important for the correct choice of pharmacotherapy.

Another diagnostic difficulty is to differentiate between nociceptive and

neuropathic pain. Sensory aberrations can be found in patients with nociceptive pain [61,62]. Furthermore, referred pain, especially if combined with sensory abnormalities, can sometimes mimic neuropathic pain.

Referred pain, characterized as perception of pain in an area distant from the site of nociceptive input (the primary pain focus), is a normal physiological phenomenon that is often reported by patients with musculoskeletal pain. Referred pain is most likely a consequence of a misinterpretation of the origin of input from the area of nociceptive stimulation. When nociceptive input becomes strong enough, neurons with projected fields in the area of referred pain become excited somewhere along the neuroaxis, giving rise to the perception of pain [59]. Results from functional magnetic resonance imaging studies show activation of the primary somatosensory cortex corresponding to the focal pain area only during perception of localized pain, whereas subjects experiencing localized and referred pain had activation of the somatosensory cortex corresponding to the central representation of the local and referred pain areas [66]. Several characteristics can be used to recognize referred pain (and to differentiate between referred pain and neuropathic pain).

First, referred pain typically has a distribution distal to the primary pain focus (with the exception of cervicogenic headache) [95] (see Fig. 15-2). Second, the intensity and distribution of referred pain are directly proportional to the pain intensity in the primary pain focus [40,41]. This phenomenon can be illustrated by a patient with lumbar pain reporting no pain in the legs when the lumbar pain is of low intensity, pain at the dorsal part of the thighs when the lumbar pain is moderate, and pain at the dorsal part of the thighs and in addition in dorsal parts of the calves when the lumbar pain is intense. Previous studies have shown larger areas of referred pain, including proximal referral of pain, in patients with whiplash-associated disorder [54], fibromyalgia [84], and osteoarthritis [10] compared with healthy controls following the same painful stimulation (i.e., pain intensities were higher in the patient groups). However, when the intensity of the evoked stimuli was calibrated to the same subjectively painful level in patients with whiplash-associated disorder (WAD) and healthy controls, still a larger distribution of referred pain, including proximal pain referral, was documented in the patient group indicating a truly different pattern of pain referral (see Fig. 15-3) [60].

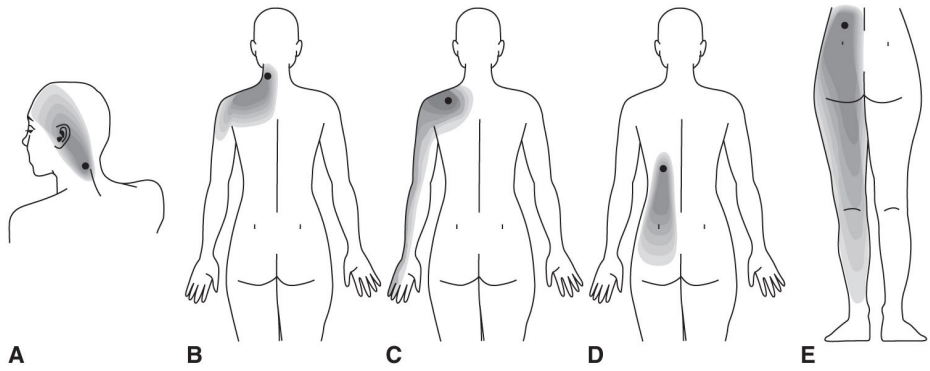

FIGURE 15-2 Typical distribution of referred pain. **A:** Primary pain focus in the upper cervical structures typically gives rise to referred pain in the form of occipital headache, spreading toward the forehead. **B:** Pain originating in the lower cervical structures is typically referred to the ipsilateral shoulder/arm/hand and the thoracic spine. **C:** Pain originating in the shoulders is typically referred to the ipsilateral arm/hand. **D:** Thoracic pain is typically referred distally to the lumbar spine. **E:** When the primary pain focus is localized at the lumbar spine, pain is typically referred to the buttocks and the thighs, calves, and/or ankles.

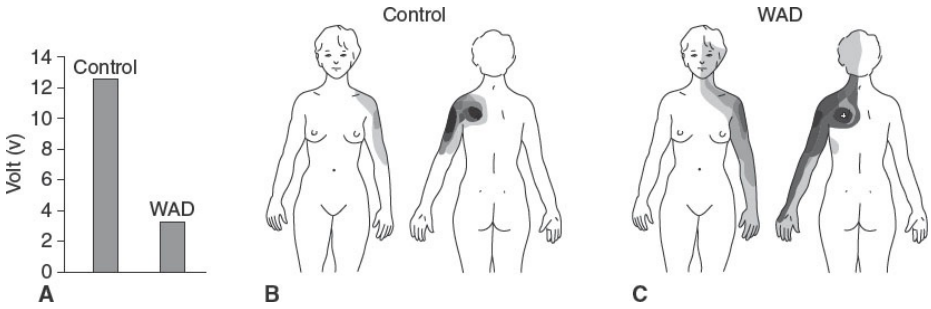

FIGURE 15-3 Increased pain sensitivity and abnormal distribution of referred pain in patients with whiplash-associated disorder (WAD). (Adapted from Kosek and Januszewska [60].) **A:** The intensity (in volts) of intramuscular (i.m.) electrical stimuli at the infraspinatus muscle that gave rise to pain ratings corresponding to 4/10 in 12 WAD patients and 12 age- and sex-matched healthy controls. The WAD patients had increased sensitivity to i.m. electrical stimulation compared with controls ($P < 0.01$). The i.m. electrical stimulus gave rise to referred pain in all subjects. **B:** The pattern of referred pain during i.m. electrical stimulation at the infraspinatus muscle in healthy controls. **C:** The pattern of referred pain during i.m. electrical stimulation at the infraspinatus muscle in WAD patients. Compared with controls, WAD patients had larger areas of referred pain ($P < 0.003$) and also had proximal pain referral, which was never seen in healthy controls.

Third, referred pain is usually perceived as diffuse and variable [58]. Sensory

abnormalities can be present in the primary pain focus as well as in the area of referred pain. The sensory aberrations are diffuse and are influenced by pain intensity, thus differing in distribution, character, and severity over time [58]. So far, no pathognomonic profile has been identified for the sensory abnormalities seen in areas of referred pain [58].

In conclusion, several characteristics differ between referred and neuropathic pain. The distribution of neuropathic pain is less variable than that of referred pain, and the sensory abnormalities in neuropathic pain states typically have a clear neuroanatomical correlate and are more consistent over time [58]. Diagnostic blocks can be used to recognize referred pain, because the referred pain stops and the sensory abnormalities normalize when the input from the primary pain focus is successfully blocked [65,98].

Neuropathic Pain

Definition of Pain

According to the most recent classification, neuropathic pain is defined as “pain arising as a direct consequence of a lesion or disease affecting the somatosensory system” [96]. Central neuropathic pain (pathology within the central nervous system) is distinguished from peripheral neuropathic pain (pathology within the peripheral nervous system). Because of the lack of a specific diagnostic tool for neuropathic pain, a grading system has been proposed for clinical and research purposes [96].

Grading System

Neuropathic pain is graded according to the following conditions:

1. Pain with a distinct neuroanatomically plausible distribution. (A region corresponding to a peripheral innervation territory or to the topographic representation of a body part in the central nervous system.)
2. A history suggestive of a relevant lesion or disease affecting the peripheral or central nervous system. (The suspected lesion or disease is reported to be associated with pain, including a temporal relationship typical for the condition.)
3. Demonstration of a distinct neuroanatomically plausible distribution by at least one confirmatory test. (As part of the neurological examination,

these tests confirm the presence of negative or positive neurological signs concordant with the distribution of pain. Clinical sensory examination may be supplemented by laboratory and objective tests to uncover subclinical abnormalities.)

4. Demonstration of a relevant lesion or disease by at least one confirmatory test. (As part of the neurological examination, these tests confirm the diagnosis of the suspected lesion or disease. These confirmatory tests depend on which lesion or disease is causing neuropathic pain.)

Definite neuropathic pain is diagnosed when all conditions (1–4) are fulfilled. A diagnosis of probable neuropathic pain requires conditions 1 and 2, plus either condition 3 or 4. A diagnosis of possible neuropathic pain requires conditions 1 and 2, without confirmatory evidence from condition 3 or 4.

PAIN OF UNKNOWN ORIGIN

Frequently, the cause of pain cannot be identified, which is especially common in patients with chronic pain localized in the musculoskeletal system. The pain is then classified as pain of unknown origin (idiopathic pain). Often, a nociceptive pain focus was initially present, but it can no longer account for the intensity and spread of pain. In many of these patients, various signs of central hyperexcitability can be found and in these cases the term “dysfunctional pain” is often used. Pain syndromes such as fibromyalgia have traditionally been classified as “pain of unknown origin.” However, the extensive documentation of central hyperexcitability (pain amplification) in fibromyalgia and the fact that centrally acting drugs have been shown to have pain-relieving effects make the term “pain of unknown origin” problematic. Until a new, more appropriate term is found for the pain in patients with central hyperexcitability, the term “dysfunctional pain” may be used (as will be the case in this chapter).

A problem with dysfunctional pain is a lack of consensus as to how to identify individual patients with central hyperexcitability. On the basis of clinical experience, certain symptom constellations are considered to indicate dysfunctional pain, although not all are specific for this kind of pain. The characteristics of dysfunctional pain are (1) increased intensity and distribution of spontaneous ongoing pain in combination with increased sensitivity to stimulus-evoked pain, without a corresponding worsening of the underlying

(peripheral) pathology; (2) after-sensations such as increased pain following palpation; (3) increased pain intensity following physical activity; and (4) increased pain during sitting or standing so that the patient reports a constant urge to change positions. Central hyperexcitability suggesting dysfunctional pain has been found in many different pain syndromes such as whiplash-associated disorder [27,28,60,82], temporomandibular disorder [67], trapezius myalgia [64], chronic low back pain (CLBP) [37], and fibromyalgia [21,56]. Studies have found that central hyperexcitability is a major negative prognostic factor in patients with whiplash-associated disorder [53,88–90]. The best-studied disorder with regard to central hyperexcitability is fibromyalgia, which is associated with multimodal allodynia/hyperalgesia [56], increased temporal summation [85,86], and dysfunction of endogenous pain inhibitory mechanisms [46,57,63].

PHARMACOTHERAPY

Pharmacological Agents Used for Pain Relief

NSAIDs, Coxibs, and Acetaminophen (Paracetamol)

Nonsteroidal anti-inflammatory drugs (NSAIDs) and coxibs have anti-inflammatory, analgesic, and antipyretic effects through inhibition of the enzyme cyclooxygenase (COX), which is involved in the transformation of arachidonic acid to prostaglandins. Prostaglandins are involved in the induction of peripheral sensitization and also have pronociceptive effects in the central nervous system. There are two main kinds of COX, COX-1 and COX-2, the latter mainly present during inflammation. The traditional NSAIDs have a nonselective inhibitory effect on COX-1 and COX-2, whereas the coxibs are selective inhibitors of COX-2. The analgesic effects of NSAIDs and coxibs are equal. The difference is that the coxibs lack the anticoagulation effects and have been reported to have a reduced number of gastrointestinal side effects compared with traditional NSAIDs, although the risk for cardiovascular side effects and renal failure are the same. Acetaminophen (paracetamol) is an analgesic and an antipyretic but lacks anti-inflammatory effects. Its mechanisms of action are not completely understood, but it is considered to have a weak, possibly indirect, COX inhibitory effect [39]. NSAIDs, coxibs, and acetaminophen/paracetamol can also potentiate the analgesic effect of opioids.

Opioids

Seventy percent of the μ-opioid receptors in the dorsal horn of the spinal cord are located on presynaptic Aδ and C fibers [15], whereas Aβ fibers lack opioid receptors. The remaining 30% are located postsynaptically on interneurons and projecting neurons [15], including the wide–dynamic-range neurons [29]. The activation of μ-opioid receptors has normally inhibitory effects, consisting of presynaptic inhibition of primary nociceptive afferents and postsynaptic inhibition of projecting neurons. The opioid receptors are synthesized in the dorsal root ganglia (in the cell bodies of Aδ and C fibers) and are transported centrally and peripherally. Nerve damage has been reported to reduce the number of opioid receptors, most likely because of impaired axonal transport [14], whereas the opioid receptors increase in the periphery during inflammation [87].

Opioids are traditionally divided into two arbitrary categories, weak and strong opioids [102]. However, it is important to remember that a high dose of weak opioids can be equivalent to treatment with the so-called strong opioids, and vice versa. Codeine and tramadol are generally considered to be weak opioids. Codeine itself lacks analgesic effects, but it is metabolized to morphine in the liver (except in approximately 9% of the population) [18]. Tramadol is a weak μ-opioid-receptor agonist and a weak reuptake inhibitor of serotonin and norepinephrine. Buprenorphine, a strong opioid, is equipotent to the weak opioids when administered transdermally (as a slow-release patch). Slow-release products (e.g., transdermal buprenorphine and oral slow-release tramadol) are believed to have a lower risk of tolerance development and abuse [50]. They provide a stable analgesic effect, even during the night, and are suited for treatment of patients with long-term pain.

There are several strong opioids, including morphine, methadone, fentanyl, hydromorphone, meperidine/pethidine, oxycodone, and buprenorphine. If patients with chronic non-cancer pain are treated with strong opioids, a fixed dose of a long-acting, extended-release opioid is recommended because it provides a more consistent analgesic effect, with less risk of end-of-dose breakthrough pain and better nighttime pain control compared with short-acting drugs [76].

Acute pain and cancer pain are often successfully treated by a combination of NSAIDs or coxibs and strong opioids. Patients with chronic nonmalignant pain constitute a more problematic group because of the risk of serious side effects and addiction or abuse. Treatment of pain with strong opioids in patients with chronic nonmalignant pain should be initiated by an experienced pain

specialist. During the titration phase, frequent treatment evaluations are necessary. Many authorities consider that a positive treatment effect of opioids in long-term nonmalignant pain includes improvements of function and quality of life in addition to pain relief [79]. A history of psychiatric disease or ongoing/previous addiction is a risk factor for psychological addiction and abuse. The patient must be informed about the risk of side effects (constipation, sedation, nausea, vomiting, and dizziness) and also told of the risk of addiction. Furthermore, the patient must be willing to discontinue medication in the case of inadequate analgesic effects or uncontrolled dose escalation.

At the initial stage of opioid therapy, a distinction needs to be made between a true analgesic effect and affective analgesia (an anxiolytic and/or euphoric effect). It is likely that a patient has a true analgesic effect if (1) a clear reduction of pain intensity is reported, (2) the duration of analgesia corresponds to the pharmacological drug effect, (3) the dose–response relationship is positive (i.e., increased analgesia with increased dose), (4) the reduced pain intensity leads to increased activity (mental and physical), and (5) the treatment leads to increased function and better quality of life. Characteristic for affective analgesia is that the patient reports that the pain intensity per se is not much different, but that he or she is no longer so bothered by the pain. Typically this phenomenon is described as “it is easier to relax” or “I do not care as much about the pain, even though it is still there.” Tolerance development is more pronounced for the affective than for the sensory, pain-reducing effect of opioids. Therefore, patients with affective analgesia are at increased risk of psychological dependence and iatrogenic drug addiction and abuse [38,55,80]. These patients should be withdrawn from opioid medication.

Opioid tolerance refers to a shorter duration and reduced intensity of the opioid effects with repeated use. In experimental settings, tolerance to respiratory suppression develops fast [81]. Tolerance for sedation, cognitive side effects, and nausea/vomiting take a longer time to develop; tolerance does not develop for opioid-induced meiosis and constipation [81]. In correctly administered opioid treatment in patients with chronic, opioid-sensitive pain states, tolerance development to the analgesic effect of the opioid is rare, and the opioid dose is basically only increased if the medical condition progresses [38,80]. However, there are exceptions in which tolerance to the analgesic effect of opioids occurs despite correct treatment. In these cases there is also a cross-tolerance to other opioids, but the cross-tolerance is incomplete [23]. This phenomenon has led to the tradition of opioid rotation, in which, when an insufficient treatment effect develops over time with one opioid, the patient is switched to another opioid [17,94]. Long-term opioid treatment always leads to

the development of physical dependence, which should not be mistaken for abuse. The meaning of physical dependence is that a quick withdrawal from opioids will lead to withdrawal symptoms. Therefore, a gradual withdrawal from opioids is always necessary following long-term use [80,81].

Opioid-induced hyperalgesia is a recently reported phenomenon and refers to the increased pain sensitivity reported in former drug addicts [68] and possibly also in pain patients following high doses of opioid therapy [20]. Former opioid addicts are reported to have an increased sensitivity to stimulus-induced pain that can remain after successful withdrawal from opioid abuse [78]. Increased pain sensitivity has also been reported in former opioid addicts on current substitution therapy with methadone or buprenorphine [24,25,33]. It is considered that these patients have a long-term (perhaps permanent) change in the balance between opioid (antinociceptive) and cholecystokinin (pronociceptive) pain regulatory mechanisms [45]. This phenomenon must be considered when former addicts are treated for acute pain following trauma or surgery, because on average they need higher doses of opioids compared with individuals who have no history of addiction in order to achieve adequate analgesia [2,32].

Serotonin and Norepinephrine Reuptake Inhibitors

The pharmacological agents in this group were originally developed for the treatment of depression and are therefore known as antidepressants (which is inappropriate from the perspective of pain treatment). Drugs with a combined reuptake inhibitory effect on serotonin and norepinephrine, tricyclic antidepressants and serotonin–norepinephrine reuptake inhibitors (SNRIs), have been reported to have analgesic effects in neuropathic pain states [34] and fibromyalgia [19]. There is also limited evidence for a beneficial effect in certain nociceptive pain states: osteoarthritis, rheumatoid arthritis, and acute low back pain [83]. The likely mechanism of action is that increased levels of serotonin and norepinephrine, two transmitter substances implicated in descending pain inhibitory pathways, increase the efficacy of endogenous pain inhibition. In support of this, deficient function of endogenous pain inhibition at baseline predicted positive response to SNRI treatment in patients suffering from neuropathic pain [103]. In addition, the positive drug effect was related to improved function of endogenous pain inhibition [103]. The analgesic effect is independent of the antidepressant effect [69]. Selective serotonin reuptake inhibitors (SSRIs) lack analgesic effects and should not be used for treatment of pain [69]. The tricyclic antidepressants have many side effects that limit their

usefulness, especially in older patients. The most common side effects are dryness of mouth, constipation, sweating, dizziness, fatigue, palpitations, orthostatic hypotension, sedation, and urine retention. The SNRIs are generally better tolerated, the main side effects being nausea, vomiting, constipation, somnolence, dry mouth, sweating, loss of appetite, and sexual dysfunction.

Anticonvulsive Medications

Gabapentin and pregabalin bind to the $\alpha_2\delta$ subunit of the voltage-dependent calcium channels and thus presynaptically reduce the release of glutamate and substance P, which in turn leads to reduced activation of postsynaptic nociceptive neurons [35]. In animal models of neuropathic pain, upregulation of $\alpha_2\delta$ subunits has been documented that corresponds to the degree of allodynia as well as to the analgesic effect of gabapentin [35]. Both drugs have the same mechanism of action, but pregabalin has a linear relationship between dose and plasma concentration, which makes titration to the proper dose easier. The drugs have a documented pain-relieving effect in neuropathic pain [34,36] and fibromyalgia [3,4,73]. The analgesic effects are not related to the anxiolytic effects of the drugs [3]. The main side effects of the anticonvulsants are dizziness, somnolence, and peripheral edema.

Practical Aspects of Pharmacotherapy

As mentioned earlier, the treatment of patients with long-term pain should always rely on the bio-psycho-social pain model, which takes the complexity of pain into account. The possibility of treating the cause of pain (with surgery or disease-modifying pharmacological treatments) must always be considered before entering the path of symptomatic pharmacological pain relief. Patients must be informed that the treatment is symptomatic so that they do not continue to take medication in the belief that it will somehow beneficially affect the medical condition. They should be encouraged to discontinue medication when the pain is no longer present, or if the drug has lost its analgesic effects. Other treatment options such as physical therapy, cognitive-behavioral therapy, and multiprofessional team rehabilitation should be considered as an alternative to, or in addition to, pharmacological treatment. It is important to realize that not all forms of chronic pain can be successfully treated with pharmacotherapy. One of the most difficult tasks of the pain physician is to withdraw ineffective pain medications even in the absence of other options for pharmacological pain relief.

The choice of drugs relies on the intensity and type of pain to be treated, as well as on the effects of the pharmacological treatment.

Pharmacotherapy for Nociceptive Pain

The choice of pharmacological treatment of nociceptive pain relies mainly on pain intensity, although NSAIDs/coxibs are preferred over acetaminophen in inflammatory pain states. Acetaminophen, NSAIDs, and coxibs are used for low and moderate pain intensities, and if the analgesia they provide is insufficient, the weak opioids are added (because of the synergistic effects of these drugs). The pharmacological treatment of severe acute pain and severe cancer pain (and in certain circumstances severe nonmalignant chronic pain) relies on the combination of acetaminophen/NSAIDs/coxibs and strong opioids. The general principle is to use the weakest possible category of drugs that give adequate pain relief.

In treatment of acute pain, the choice of drugs relies on the expected pain intensity following an injury or medical procedure, such as surgery. Patients should be provided with a sufficient amount of pain medication for the expected duration of pain and should be carefully instructed when and how to discontinue treatment and whom to contact in case of problems.

In cases when long-term treatment is likely, slow-release preparations of an opioid should be considered because of the lower risk of tolerance development and abuse potential. In patients with disturbed sleep due to nocturnal pain, slow-release preparations are preferred because of their longer effect duration (reducing the need for further analgesic intake at night). Patients on weak opioids who experience insufficient pain relief, yet have an analgesic effect with a clear dose–response relationship, can be considered for strong opioids (see the previous section). These patients are encouraged to continue with acetaminophen (or NSAIDs/coxibs) but to discontinue the weak opioid. Generally the dose of the strong opioid is titrated to the lowest effective dose, and a slow-release preparation is preferred. In patients with long-term nonmalignant pain who are taking long-acting opioids, the use of short-acting opioids as rescue medications during pain exacerbation should be avoided (to reduce the risk of opioid tolerance and abuse).

The treatment of long-term nonmalignant pain with strong opioids increases the demands on the physician to monitor treatment effects. Treatment effects should be evaluated not only for reductions in pain, but also for improvements in function and quality of life [52,79]. It is the responsibility of the physician to inform the patient not only about potential side effects and risk of addiction, but

also to have an understanding with the patient regarding the estimated duration of treatment and under which circumstances the treatment with strong opioids will be discontinued. Generally, long-term treatment with opioids is not inefficacious and not well tolerated [51].

Pharmacotherapy for Pain of Unknown Origin and Central Hyperexcitability

Pain of unknown origin is difficult to treat because the pathophysiological mechanisms are unknown. Naturally, no drugs have the indication of treatment of pain of unknown origin, although tricyclic antidepressants such as amitryptiline are commonly used. Pharmacotherapy of dysfunctional pain, that is, pain in patients with documented central hyperexcitability such as in fibromyalgia, has been studied in several randomized, double-blind, placebo-controlled trials. The recommended drugs are similar to those used for treatment of neuropathic pain, described below. A special difficulty arises when treating patients who initially had nociceptive pain (and responded to antinociceptive treatment) but who in time developed signs of central hyperexcitability (i.e., they probably developed dysfunctional pain). In these patients, the initially effective medication usually loses its pain-relieving effects, which is in accordance with animal studies showing a decreased effect of opioids in animals with central hyperexcitability [30]. These patients should be encouraged to discontinue the ineffective medication. Theoretically, such patients would be likely to respond to similar pharmacotherapeutic strategies as those used to treat the dysfunctional pain of fibromyalgia, which is supported by studies showing positive effects of SNRIs also in patients suffering from osteoarthritis and chronic low back pain [83].

As mentioned, a great number of randomized controlled trials have been completed in fibromyalgia patients, and treatment guidelines, including pharmacotherapy, have been published [19]. Tricyclic antidepressants, such as amitryptiline, have been shown to have a beneficial effect on pain, sleep, fatigue, stiffness, and tenderness [5] in fibromyalgia patients. Several double-blind, placebo-controlled studies have reported that SNRIs such as duloxetine [6,7] and milnacipran [42,99] reduce pain, tenderness, and stiffness and improve function and quality of life in fibromyalgia patients. These effects were independent of the baseline levels of anxiety or depression and did not relate to the improvement of these psychological symptoms [6,7]. However, there is evidence that the treatment effect might be higher in patients with shorter duration of pain

and FM [48].

The SSRIs lack convincing pain-relieving effects in fibromyalgia [77]. The anticonvulsants pregabalin [3,26,73] and gabapentin [4] had beneficial effects on pain, sleep, and fatigue in fibromyalgia patients. Combination treatments have not been evaluated in fibromyalgia, but in clinical practice the combination of SNRIs and anticonvulsants has shown promising potential, with good treatment effects and reduced side effects (due to lower doses).

Tramadol (used alone or in combination with acetaminophen/paracetamol) has been documented to relieve pain and improve function in fibromyalgia patients [13]. There are no data assessing the effects of acetaminophen (monotherapy), codeine, dextropropoxyphene, buprenorphine, and strong opioids in dysfunctional pain syndromes. The use of strong opioids to treat the pain in fibromyalgia is generally not recommended [19], although there are cultural differences in treatment traditions.

Pharmacotherapy for Neuropathic Pain

Treatment recommendations regarding peripheral neuropathic pain mainly rely on studies of patients with painful diabetic polyneuropathy and herpes zoster under the assumption that the same treatments will also be effective for other peripheral neuropathic pain states (with the exception of trigeminal neuralgia).

The first line of recommended treatments is tricyclic antidepressants, SNRIs, or anticonvulsive medications (pregabalin or gabapentin) and topical lidocaine (for patients with small areas of mechanical allodynia). The second-line treatments are tramadol and opioid analgesics [34]. Combination therapy using SNRIs (duloxertone) and anticonvulsants (pregabalin) has been shown to be safe, effective, and well tolerated [92]. However, there are indications that high-dose monotherapy might be more efficient in patients with severe pain, whereas combination therapy might be more beneficial in patients with more moderate pain intensities [16]. SNRIs and anticonvulsive medications have positive effects on sleep and quality of life, in addition to their pain-relieving effects. The pain-relieving effects of the antidepressants are not dependent on the antidepressant (mood) effects of the drugs, nor do SSRIs have positive pain-relieving effects [69]. Most studies indicate a lower efficacy of opioids in neuropathic compared with nociceptive pain. Long-term follow-ups have indicated that only a minority of patients continue with strong opioids after 1 year, generally because of intolerable side effects [51]. The relative inefficacy of opioids for the treatment of neuropathic pain, compared with nociceptive pain, has been discussed. The reduction of spinal opioid receptors due to nerve damage, the presence of Aβ-

fiber-mediated pain (which is not responsive to opioids), and increased cholecystokinin- and/or NMDA-dependent activity (i.e., central sensitization) have all been proposed as possible explanations.

SUMMARY

In summary, medical management of pain requires a careful examination of the pain problem to classify pain as nociceptive, neuropathic, or pain of unknown origin and to recognize cases with central hyperexcitability. Understanding the cause of the pain is essential to adequate treatment. A bio-psycho-social approach is likely to be necessary with chronic pain conditions, particularly when they are complex and difficult to treat. The choice of pharmacological treatments depends on the intensity and type of pain treated, and the best approach is to use the weakest possible category of drugs that give adequate pain relief.

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CHAPTER 16

Psychological Approaches in Pain Management

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Effective treatments for patients with chronic pain have not kept pace with advances in understanding of anatomy and neurophysiology. Despite the development of potent medications, sophisticated neuroaugmentation technologies (e.g., spinal cord stimulators), advanced surgical procedures, a diverse set of somatic treatments (e.g., transcutaneous electric nerve stimulation, diathermy), and a range of complementary approaches (e.g., acupuncture, meditation, yoga, tai chi), most people with chronic pain continue to experience significant levels of pain regardless of the treatments they receive [62]. Chronic pain, similar to other chronic diseases, makes significant demands on people's lives, and those affected vary widely in how well they cope with the demands that confront them, adapt to the symptoms, and accommodate to the limitations imposed.

An expansive literature demonstrates the important contributions of psychosocial and behavioral factors to symptom onset, magnification, maintenance, accommodation, and response to treatment [15,27]. Based on current understanding of the roles of cognitive, affective, and behavioral factors, a set of psychological approaches and treatments have been developed to assist in symptom management and to foster adaptation. Many of these treatments have long histories (e.g., hypnosis, psychotherapy) in treatment of people with chronic pain. These treatments have been applied to a number of chronic pain diagnoses (Table 16-1).

Although psychological approaches have been used as alternatives to pharmacological and somatic treatments, in most circumstances they are used in conjunction with traditional medical interventions and as integrative components within comprehensive, interdisciplinary rehabilitation programs. In this chapter we will emphasize an important distinction between psychological *perspectives* on chronic pain and specific psychological *treatments*, provide a description of

the predominant psychological perspectives and most commonly used methods, and review the evidence for the effectiveness of the various techniques for a diverse set of diagnoses (see Table 16-1). Due to space limitations we will only be able to highlight central features of the perspectives and treatment methods.

TABLE 16-1 **Psychological Treatment Studies Included**

Diagnoses/Site of Pain	*N* Studies	*N* Patients
RA	13	837
Low back	11	601
TMD	11	457
Mixed	8	416
OA	5	313
OA/RA	2	1350
FM	2	171
Upper limb	2	193
Disability-related	1	33
Sickle-cell disease	1	37
Total	56	4378

Note: These data do not include studies in which psychological approaches are integrated within comprehensive rehabilitation programs. The primary outcomes in these studies are pain reduction and some also included outcomes related to physical and emotional functioning.

Abbreviations: RA, rheumatoid arthritis; TMD, temporomandibular disorders; OA, osteoarthritis; FM, fibromyalgia syndrome.

Source: Adapted from meta-analyses and systematic reviews Campbell et al. [8], Holroyd et al. [24], McCracken and Vowles [33].

DISTINCTION BETWEEN PSYCHOLOGICAL APPROACHES AND PSYCHOSOCIAL TREATMENTS

Several prominent psychological perspectives have guided much of the thinking about chronic pain and subsequent treatments that have evolved, in particular the (1) psychodynamic, (2) operant conditioning (behavioral), and (3) cognitive-behavioral perspectives. In addition to treatments that are directly related to these perspectives, a set of treatment techniques have been developed that are often combined (e.g., biofeedback plus relaxation; hypnosis plus guided imagery plus relaxation) and that may not be directly associated with any one perspective (e.g., hypnosis or biofeedback). The characteristics of these treatments are briefly highlighted in Table 16-2. We will provide an overview of each of these perspectives and treatment strategies and describe the treatments that have been

developed that follow from the conceptual models (Table 16-3). However, it is important to acknowledge that the perspectives themselves are quite broad and may include any number of cognitive, behavioral, or psychotherapeutic techniques [49,52].

Perhaps more important than the details of each technique are the specific objectives that each of the techniques is used to accomplish (e.g., to increase perception of control, extinguish maladaptive behaviors, or uncover unconscious motivation). The same technique, however, may be used to accomplish different or overlapping objectives. For example, exposure to avoided activities, a common component of operant conditioning treatments, may be conceptualized as a way to help patients learn that the performance of previously avoided activities may not produce the anticipated negative consequences (e.g., promote pain or exacerbate injury). Thus, exposure treatment can provide corrective feedback. From this perspective, the treatment is designed to alter the reinforcement contingencies—activity is not "punished" by pain, and thus avoidance of activity will be extinguished. However, exposure might also be viewed from a cognitive-behavioral perspective, whereby it is conceptualized as a way to help patients increase their sense of self-efficacy by providing success in performance of previously avoided tasks and reduce anticipation of pain or injury following performance of the activity. In this conceptualization, the use of a behavioral technique is designed not only to change behavior but to alter patients' beliefs about themselves and their capabilities—they are not helpless. Of course, these two mechanisms are not mutually exclusive. Similarly, biofeedback may be viewed as a means of modifying some maladaptive physiological response, but practicing with biofeedback devices may also change patients' perceptions of control over their bodies, whether or not it actually influences physiological mechanisms believed to be associated with the presence of pain. Throughout the remainder of this chapter, it is important to keep in mind the distinction between the psychological perspectives underlying treatment and the details of the treatment modalities themselves.

TABLE 16-2 Psychological Interventions

Psychodynamic therapy: focus on uncovering unresolved conflicts that are believed to contribute to pain

Behavior therapy: managed approach to behavior change using the basic concepts and principles of behavioral psychology

Cognitive-behavior therapy (CBT): primary focus on changing cognitive activity to achieve changes in behavior, thoughts, and emotions. Two broad classes: (1) coping skills training and (2) cognitive therapy

Relaxation: attempt to teach patients how to reduce general levels of physiological arousal or arousal in a specific body part or location (e.g., autogenic training, progressive muscle relaxation)

Biofeedback: involves measuring an individual's quantifiable bodily functions (e.g., blood pressure, heart rate, skin temperature, sweat gland activity, muscle tension, electrical activity in the brain) using noninvasive electrical devices that record and amplify physiological signals and conveying the information to the patient in real time. The intent is to raise the patient's awareness and conscious control of their unconscious physiological activities. By providing the patient access to physiological information about which he or she is generally unaware, biofeedback allows patients to gain control of physical processes previously considered an automatic response of the autonomic nervous system that may exacerbate their pain

Hypnosis/hypnotherapy: the patient is guided by the hypnotherapist to respond to suggestions for changes in subjective experience, alteration in perception, sensation, thought, or behavior. Teaches skills that are designed to alter the experience of pain and suffering outside the therapy session

Meditation: the "intentional self-regulation of attention," a systematic inner focus on particular aspects of inner and outer experience

TABLE 16-3 Psychological Perspectives and Illustrative Treatments

Perspective	Techniques
Psychodynamic perspective	Insight-oriented psychotherapy
Behavioral perspectives	Reinforcement, pacing, goal-setting, exposure, relaxation
Cognitive-behavioral perspective	Cognitive restructuring, problem solving, coping skills training, acceptance
Other	Motivational interviewing, biofeedback, hypnosis, imagery, meditation, supportive counseling

Note: A number of techniques listed may be used in more than one perspective with the intent varying. The techniques listed under "other" can be used independent of any particular theoretical perspective or in combination.

THE PSYCHODYNAMIC PERSPECTIVE

Theoretical Perspective

From the psychodynamic perspective, symptoms serve a purpose, and treatment is designed to help the patient identify the unconscious meaning of symptoms that occur in the absence of or in disproportion to physical pathology. In the later 1800s and early 1900s, Sigmund Freud proposed that the underlying motivational force is the gratification of biologically based, instinctual drives. In classical psychoanalysis, chronic pain that cannot be explained by outright tissue

damage can be viewed as resulting from an unconscious "drive" that the individual is unable to gratify in a socially acceptable manner. When such repressed urges threaten to emerge into consciousness, severe anxiety results, and the resolution, however maladaptive it may appear to be, is a psychic compromise that can include the development of physical and emotional symptoms that protect the patient from the trauma created by the awareness of unacceptable drives. In short, symptoms serve a purpose.

Insight-Oriented Treatments

Insight-oriented approaches are predicated on the belief that chronic physical pain may be somatic presentations of emotional distress and that nonconscious factors will influence both the onset and maintenance of symptoms. Psychodynamic therapy is most commonly used when psychosocial risk factors appear to play a role in pain symptoms, when emotional changes occur during severe and protracted pain, or when the goals of therapy are not only to relieve symptoms of pain, but also to promote long-term adaptation [4].

The overriding goal of psychoanalytic treatment is for patients first to become aware of and later to renounce unconscious impulses and conflicts and then to obtain partial gratification through sublimation in adult roles and relationships. Attempts are made to help patients gain insights into the reasons that pain developed and persists. Maintenance of symptoms may serve as a means of protecting the patient from unacceptable impulses or to obtain some benefit such as support or avoidance of undesirable interactions.

Although insight-oriented psychotherapy may be useful with selected individuals [4], to our knowledge, no adequate, randomized clinical trials have been published demonstrating its efficacy for people with chronic pain problems. Although the model described may be applicable in specific circumstances, the usefulness of insight-oriented psychotherapy for patients with chronic pain seems limited.

OPERANT CONDITIONING

Theoretical Perspective

In the operant formulation, pain is viewed as a subjective experience that can never be observed directly. Thus, behavioral manifestations of pain—"pain

behaviors" (overt expressions of pain, distress, and suffering)—that are observable are key to understand and treat patients, rather than focus exclusively on nociception. The model proposes that through external contingencies of reinforcement, acute pain behaviors, such as limping to protect a wounded limb from producing additional nociceptive input, can evolve into chronic pain problems. Pain behaviors may be positively reinforced directly, for example, by attention from a spouse or health care provider. They may also be maintained by negative reinforcement through the escape from noxious stimulation by using drugs, resting, or avoiding other activities and responsibilities that the patient may consider undesirable, such as work or exercise (Table 16-4).

TABLE 16-4 **Operant Schedules of Reinforcement**

Schedule	Consequences	Probability of Behavior Recurring
Positive reinforcement	Reward the behavior	More likely
Negative reinforcement	Prevent or withdraw aversive results	More likely
Punishment	Punish the behavior	Less likely
Neglect	Prevent or withdraw positive results	Less likely

In addition to external reinforcement for pain behaviors, "well behaviors" (e.g., working, exercising) may not be sufficiently reinforced or reinforcing. This lack of reinforcement allows more rewarding pain behaviors to be maintained. Pain behaviors originally elicited by organic factors may respond to reinforcement from environmental events and may therefore be maintained. Fordyce [13] proposed that for this reason, pain behaviors might persist long after the initial cause of the pain is resolved or greatly reduced. The operant conditioning model does not concern itself with the initial cause of pain. Rather, it considers pain an internal subjective experience that may be maintained even after its initial physical basis is resolved.

The emphasis on maintaining factors shares some overlap with the psychodynamic perspective. The difference, however, is that from the psychodynamic perspective, symptoms are associated with unconscious intrapsychic conflicts, whereas from the operant perspective, maintenance and generalization result from reinforcement contingencies, as described below.

Operant Treatment

Operant approaches focus on the extinction of pain behaviors and increase in the number and nature of well behaviors. Therapists focus on withdrawal of positive

attention for pain behaviors while increasing positive reinforcement of well behaviors (e.g., activity). Following operant theory, treatment does not seek to uncover the etiology of symptoms but focuses on the maintenance of pain behaviors and the deficiency of appropriate well behaviors. In treatment, pain behaviors are identified, as are their controlling antecedents and consequent reinforcers or punishments, such as overly solicitous behaviors by a spouse [48,56].

The efficacy of operant treatment has been demonstrated in a number of studies of persons with various chronic pain disorders, including low back pain (e.g., references [63, 66]) and fibromyalgia syndrome [55]. Based on a meta-analysis of treatment studies for chronic pain, Morley et al. [37] reported that the effect size of behavior therapy varied for different outcomes ranging from 0.33 for pain reduction to 0.62 for affective distress, other than depression, where the effect size was quite small and negative (0.01) compared with control treatments, often standard care (see Tables 16-5 and 16-6).

TABLE 16-5 **Effectiveness of CBT, BT, BFB, RLX versus Waiting-List Control**

Domain	*N*	Mean ES	95% CI	Z
Pain experience	28	0.40	0.22–0.58	4.28
Mood/depression	24	0.36	0.13–0.59	3.11
Mood/other	16	0.52	0.19–0.84	3.10
Cog cop & neg appr	16	0.50	0.27–0.73	4.20
Cog cop & pos appr	11	0.53	0.28–0.78	4.20
Behav expression	12	0.50	0.22–0.78	3.49
Behav activity	14	0.46	0.25–0.72	4.34
Soc role funct/interf	25	0.60	0.44–0.76	7.28

Abbreviations: N, number of studies; CBT, cognitive-behavior therapy; BT, behavior therapy; BFB, biofeedback; RLX, relaxation; cog cop & neg appr, cognitive coping and negative appraisal; cog cop & pos appr, cognitive coping and positive appraisal; soc role funct/interf, social role functioning and interference.

Source: Adapted from Morley et al. [37].

TABLE 16-6 **Effectiveness of CBT, BT, BFB, RLX versus Treatment Controls**

Domain	*N*	Mean ES	95% CI	Z
Pain experience	22	0.29	0.11 to 0.46	3.21
Mood/depression	15	–0.14	–0.32 to 0.04	–1.52
Mood/other	16	0.05	–0.27 to 0.37	–0.30
Cog cop & neg appr	14	0.17	–0.08 to 0.42	1.35
Cog cop & pos appr	15	0.40	–0.21 to 0.62	3.60
Behav expression	11	0.27	0.08 to 0.47	2.76
Behav activity	0		----------	----------
Soc role funct/interf	14	0.17	–0.08 to 0.34	1.62

Abbreviations: N, number of studies; CBT, cognitive-behavior therapy, BT, behavior therapy; BFB, biofeedback; RLX, relaxation; cog cop & neg appr, cognitive coping and negative appraisal; cog cop & pos appr, cognitive coping and positive appraisal; soc role funct/interf, social role functioning and interference.

COGNITIVE-BEHAVIORAL PERSPECTIVE

Theoretical Perspective

From the cognitive-behavioral perspective, thoughts and emotions are thought to play a key role in potentiating and maintaining stress and physical symptoms. Patients are assumed to have negative perceptions regarding their abilities, the impact of environmental factors, the consequences of their behavior, and lack adequate coping skills to manage both physical and emotional stressors. These ineffective coping mechanisms have been developed over a lifetime of experience and become automatic, and thus the overarching goal of therapy is to help patients identify these negative perceptions, improve their coping skills and increase self-efficacy beliefs, and increase self-management of problems associated with symptoms.

TABLE 16-7 **Assumptions of the Cognitive-Behavioral Perspective**

- People are active processors of information and not passive reactors
- Thoughts (e.g., appraisals, expectancies, beliefs) can elicit and influence mood, affect physiological processes, have social consequences, and can also serve as an impetus for behavior; conversely, mood, physiology, environmental factors, and behavior can influence the nature and content of thought processes
- Behavior is reciprocally determined by *both* the individual and environmental factors
- People can learn more adaptive ways of thinking, feeling, and behaving
- People should be active collaborative agents in changing their thoughts, feelings, behavior, and physiology

Source: Adapted from Turk and Meichenbaum [60].

Cognitive-Behavioral Treatment

One of the problems describing cognitive-behavioral therapy (CBT) is that it has become a generic term that includes a range of different cognitive and behavioral techniques [27, 52]. We describe the general approach to treatment from the general cognitive-behavioral perspective; however, although the perspective remains constant, the specific techniques and modalities that are used may vary substantially.

Four key components of CBT have been described [12,56]: (1) education, (2) skills acquisition, (3) skills consolidation, and (4) generalization and maintenance. The "education" component focuses on helping patients challenge their negative perceptions regarding their abilities. It helps patients to manage pain through "cognitive restructuring," by making them aware of the role that thoughts and emotions play in potentiating and maintaining stress and physical symptoms. Cognitive restructuring includes identification of maladaptive thoughts during problematic situations (e.g., during pain exacerbations or stressful events), introduction and practice of coping thoughts and behaviors, shifting from self-defeating to coping thoughts, practice of positive thoughts, and home practice and follow-up. The therapist encourages patients to test the adaptiveness of their thoughts, beliefs, expectations, and predictions. The crucial element is bringing about a shift in the patient's repertoire from well-established, habitual, and automatic but ineffective responses toward systematic problem-solving and planning, control of affect, behavioral persistence, and disengagement from self-defeating situations when appropriate (Table 16-7).

The goal of "skills acquisition" and "consolidation" is to help people learn and, importantly, practice new pain management behaviors and cognitions, including relaxation, problem solving, distraction methods, activity pacing, and communication. Therapists use education, didactic instruction, Socratic questioning, and role-playing techniques, among other strategies. The techniques, however, are less important than the general emphasis on self-management that is derived from experience using various techniques (some of which are described below). Patients may learn best from observing the outcomes of their own efforts rather than by instruction alone. Often CBT is carried out in a group context where the therapist can use the support of other patients and also have patients interact with each other to assist in providing alternative ways of thinking and behaving.

Finally, "generalization and maintenance" are geared toward solidifying skills and preventing relapse. Homework is an essential ingredient of CBT. Once patients have been taught and have practiced self-management skills within the

therapeutic context, it is essential that they practice them in their home environment where the therapist is not present to guide and support them. The difficulties that will inevitably arise when these attempts are made at home become important topics for discussion and further problem solving during therapeutic encounters. In this phase, therapists assist patients to anticipate future problems and high-risk situations so that they can think about and practice the behavioral responses that may be necessary for adaptive coping. The goal during this phase, then, is to enable patients to develop a problem-solving perspective where they believe that they have the skills and competencies to respond in appropriate ways to problems as they arise. In this manner, attempts are made to help patients learn to anticipate future difficulties, develop plans for adaptive responding, and adjust their behavior accordingly.

Some of the cognitive and behavioral techniques described require specialized training, but the cognitive-behavioral perspective is relevant regardless of the specific training of healthcare providers. Variants and modifications of CBT have been demonstrated to be readily transferable and effective when delivered by physical therapists (e.g., references [5,14,41,42]) and nurse practitioners [7] who have been trained by psychologists.

Despite the tactical problem related to differences in the specific therapeutic elements of CBT interventions, research supports the efficacy of CBT interventions for reducing pain and improving physical and psychological functioning in adults and children with persistent pain [10, 43], at least modestly and comparable to other treatments [10]. But the results are relatively modest and are not consistent across studies, which may relate to the specific content, mode of delivery, duration of treatment, and extent of therapist training [10, 36]. Few studies have directly compared the efficacy of CBT with and without standard care, which often consists of medication and physical therapy.

With this overview of the CBT approach, we will discuss specific techniques that can be incorporated with CBT and operant behavior therapy. To reiterate, the primary objective of these techniques is enhancement of patients' sense of self-efficacy by increasing a sense of control to combat the feelings of helplessness and demoralization often felt by people with chronic pain.

ADDITIONAL PSYCHOLOGICAL APPROACHES

Relaxation

Many relaxation techniques exist, and there is a long history of their use in health care. The literature is inconsistent as to which techniques are the most effective, and there is no evidence that any one method is more effective than any other. Moreover, the different components may be synergistic. The key message to the patient is that a broad spectrum of approaches is available, and no particular method is more efficacious. Common approaches involve the use of breathing techniques, guided imagery, and meditation to help patients obtain a state of relaxation. It is most important to help patients learn which ones will be most helpful by trying a variety of techniques. Clinicians may also note that no one technique is effective for all people all of the time: hence, knowledge of a range of methods may be the best approach. It is important to acknowledge that these methods are skills that require practice to become more proficient. Other than in treatment of chronic headache, relaxation is most commonly used as one modality within a comprehensive treatment plan.

Guided Imagery

Although guided imagery is a common component of relaxation exercises, it is also used to help patients achieve a sense of control, and, importantly, to distract themselves from pain and accompanying symptoms. This modality involves the generation of different mental images, evoked either by oneself or with the help of the practitioner. When patients with chronic pain are experiencing pain exacerbation, they can use imagery with the goals of redirecting their attention away from their pain and achieving a psychophysiological state of relaxation. The most successful images involve all of the senses (vision, sound, touch, smell, and taste). Some people, however, may have difficulty generating images and may find it helpful to listen to a taped description or purchase a poster on which to focus their attention as a way of assisting their imagination.

Although guided imagery has been advocated as a stand-alone intervention to reduce presurgical anxiety and postsurgical pain, and to accelerate healing [19], it is most often used in conjunction with other treatment interventions such as relaxation and as a coping strategy taught within the context of CBT.

Biofeedback

Biofeedback is a self-regulatory technique. The assumption with regard to biofeedback treatment is that the level of pain is maintained or exacerbated by autonomic nervous system dysregulation, believed to be associated with the

production of nociceptive stimulation. The primary objective of biofeedback is to teach people to exert control over their physiological processes to assist in re-regulating the autonomic nervous system. When people are treated with biofeedback, they receive information about their physiological processes via biofeedback equipment, and they are taught through this feedback to regulate these processes. These monitored physiological processes may include skin conductance, respiration, heart rate, heart rate variability, skin temperature, brain wave activity, and muscle tension. In addition to the physiological changes that can result from biofeedback, patients gain a sense of control over their bodies. Given the high levels of helplessness observed in people with chronic pain problems, the perception of control may be as important as the actual physiological changes observed (e.g., reference [24]).

Biofeedback has been used successfully to treat a number of chronic pain states such as migraine and tension-type headaches, chronic back pain, chronic myofascial pain, temporomandibular disorders, irritable bowel syndrome, and fibromyalgia, either as primary treatment or within the broader context of CBT integrated within rehabilitation programs [3,16,34,40]. In one meta-analysis of biofeedback for migraine, Nestoriuc and Martin [40] included 55 studies that they judged to be of relatively high quality and found an effect size of 0.58 for prevention of migraine episodes compared with control conditions. What is particularly impressive is that these results were maintained for up to 17 months following treatment. Several studies have compared biofeedback with prophylactic migraine medication (propranolol) and found that biofeedback was as effective as the medication, with the two treatments having a synergistic effect [22]. The effect sizes for biofeedback for diagnoses other than chronic headache are also impressive, although the number of studies is much smaller. Morley [36] determined that for pain, the effect sizes for biofeedback compared with control were moderate, 0.52 (based on only one study).

Meditation

Meditation is defined as the “intentional self-regulation of attention,” a systematic inner focus on particular aspects of inner and outer experience [17]. There are many forms of meditation, although most research has focused on transcendental meditation (TM) and Zen or mindfulness meditation [1,27,30,54,69] and mindfulness-based stress reduction [5,51].

TM requires concentration; it involves focus on any one of the senses, like a zoom lens, on a specific object. For example, the individual repeats a silent word or phrase (“mantra”) with the goal of transcending the ordinary stream of

thought [2,3]. Mindfulness meditation is the opposite of TM in that its goal is attempting awareness of the whole perceptual field, like a wide-angle lens. Thus, it incorporates focused attention and whole-field awareness in the present moment. For example, the individual observes without judgment his or her thoughts, emotions, sensations, and perceptions as they arise moment-by-moment [27,28]. Bonadonna [6] proposed that individuals with chronic illness have an altered ability to concentrate; therefore, TM may be less useful than mindfulness meditation when one is sick. Attention and awareness of discomfort or suffering is another part of human experience; as such, rather than be avoided it is to be experienced and explored [5].

Mindfulness meditation reframes the experience of discomfort in that physical pain or suffering becomes the object of meditation. In a recent randomized controlled trial comparing the efficacy of mindfulness meditation in chronic pain patients relative with a wait-list control group, mindfulness meditation was found to reduce general anxiety, depression, and quality of life, and improve feelings of control over acceptance of pain [20]. The mindfulness mediation did not, however, reduce pain severity relative to the wait-list control group.

Meditation has captured the attention of medicine, psychology, and neurocognitive sciences. This interest has arisen in part because experienced meditators demonstrate reduced arousal to daily stress, better performance of tasks that require focused attention, and other health benefits [29,31,32]. Studies have found that when combined with other therapies, mindfulness-based interventions that are often extended into another CBT-based intervention—Acceptance and Commitment Therapy [33]—have decreased pain symptoms, increased healing speed, improved mood, decreased stress, contained healthcare costs, and decreased visits to primary care [3,18]. However, it is premature to draw any conclusions from the few, small outcome studies that have been reported [65].

Hypnosis

Hypnosis has been defined as a natural state of aroused attentive focal concentration coupled with a relative suspension of peripheral awareness. There are three central components in hypnosis: (1) absorption, or the intense involvement in the central object of concentration; (2) dissociation, where experiences that would commonly be experienced consciously occur outside of conscious awareness; and (3) suggestibility, in which persons are more likely to accept outside input without cognitive censoring or criticism [53].

Hypnosis has been used as a treatment intervention for pain control at least since the 1850s. It has been shown to be beneficial in relieving pain for people with headache, burn injury, arthritis, cancer, and chronic back pain [11,25,27,35,45,58]. As with relaxation techniques, imagery, and biofeedback, hypnosis is rarely used alone in chronic pain, although it has been used independently with some success with cancer patients [46]; practitioners often use it concurrently with other treatment interventions.

Elkins et al. [11] identified 13 controlled studies evaluating the efficacy of hypnosis. In general, hypnosis was significantly more effective than no-treatment comparison groups in reducing pain. However, these reviewers found few studies that compared hypnosis with credible comparison treatments, and so it is impossible to rule out the effects of attention and participation in a study (expectation and regression to the mean). In addition, discrepancies with regard to the methods used to induce hypnosis make it difficult to accurately evaluate efficacy [46].

GENERAL COMMENTS ABOUT THE EFFICACY OF PSYCHOLOGICAL APPROACHES

Early studies evaluating the efficacy of psychological approaches focused on whether treatments were comparable to other therapeutic options, and as suggested above, the clinical outcomes always tended to support the usefulness of psychological approaches and treatment modalities [12]. Although only modest improvements in pain-related outcomes were observed, analgesic medication use, physical incapacity, health care utilization, and disability rates showed marked reductions [23,50].

More recently, the increased availability of randomized clinical trials, as well as refined analytic techniques, has led to a large number of meta-analyses and systematic reviews (e.g., references [8–11,21,37]). The results of these meta-analyses with adult patients came to somewhat similar conclusions for children —as a group, psychological treatments have modest benefits in improving pain, physical, and emotional functioning [44].

Although in general the results of the meta-analyses support only modest benefit, it is important to acknowledge once again that any improvement in outcomes from psychological treatments probably occurs in addition to benefits already being realized from standard care. With few exceptions (e.g., reference [22]), investigators providing combination treatments that incorporate both

medical and psychological treatments have not attempted to differentiate the synergistic effects.

Effect sizes will also vary depending on what outcome measures are used. There is some debate as to the most appropriate outcomes in clinical trials of chronic pain. At first glance it might seem obvious that it should be reduction in pain intensity. However, there is growing acknowledgment of the importance of other outcomes such as physical functioning, emotional functioning, health-related quality of life, and patient satisfaction [59]. “Cherry-picking” selected outcomes that support the efficacy of the treatment is not appropriate. Multiple outcomes are important, and investigators evaluating treatment outcomes must consider all that are relevant and balance the results obtained to base conclusions on treatment success.

Although psychological treatments have been found to be helpful for a number of individuals, there are some for whom they are not beneficial. Investigators are just beginning to explore different aspects of CBT to answer the question “what works for whom?” [58,60,67]. Several studies have begun to explore the characteristics of patients who respond to psychological treatments in general and specific psychological treatments [20,57,61].

Turner et al. [64] found that the mediators of improvement in pain and activity 1 year after completing CBT were cognitive variables including patients’ perceptions of control, disability, self-efficacy, harm, and catastrophizing and rumination. Individual patients may learn coping skills and improve feelings of control and self-efficacy through different types of treatments. Jensen and colleagues [26] found that baseline electroencephalogram-assessed theta oscillations predicted response to hypnosis and meditation in participants with spinal cord injury and chronic pain. By identifying factors that allow treatment matching, better effect sizes may be realized.

Importantly, as noted, none of the currently available pharmacological, medical, or psychological treatments are able to provide cures for the majority of people who experience persistent pain, although many can provide reductions in symptoms and improvements in physical and emotional functioning [62].Consequently, successful pain treatment involves helping individuals learn skills that foster self-management of residual symptoms and lives in general.

However, significant problems can arise related to adherence to self-management programs and maintenance of initial positive benefits over long periods of time—years if not decades. Studies that have examined maintenance of lifestyle changes (e.g., weight loss, smoking reduction, reduction of substance abuse) have demonstrated significant relapse rates. Thus, strategies are needed to facilitate adherence to long-term change. One approach to addressing problems

with long-term maintenance is to make use of sophisticated and rapidly evolving technologies. The evolution of web-based programs and patient communities, smartphone applications, use of e-mail communication, and other service delivery platforms offer opportunities that can address both treatment barriers and issues of maintenance and generalization [39,47], often with the added benefits of convenience and privacy [38]. Findings from a number of preliminary studies support the potential of these approaches with adults [49,68] and adolescents [44]. A machine will not likely replace clinicians but can supplement what is done more directly in the clinic. Research is needed to determine how to take advantage of the possibilities and to evaluate various parameters that can be manipulated in these systems.

SUMMARY AND CONCLUSIONS

Pain that persists over time should not be viewed as either solely physical or solely psychological. Rather, the experience of pain is a complex amalgam maintained by an interdependent set of biomedical, psychosocial, and behavioral factors, whose relationships are not static but evolve and change over time. The various interacting factors that affect a person with chronic pain suggest that the phenomenon is quite complex and requires a perspective that takes into consideration cognitive factors (beliefs, attitudes, expectancies, and perceptions of self-efficacy), emotional aspects, and behavioral (social environment) factors and prior learning history as well as genetic and physical contributors to the pain experience—a biopsychosocial perspective.

From the biopsychosocial perspective, the interaction among the factors enumerated above combines to produce the subjective experience of pain [12]. There is a synergistic relationship whereby psychological and socioenvironmental factors can modulate nociceptive stimulation and the response to treatment. In turn, nociceptive stimulation can influence patients' appraisals of their situation and the treatment, their mood states, and the ways they interact with significant others, including medical practitioners. An integrative, biopsychosocial model of chronic pain needs to incorporate the mutual interrelationships among physical, psychological, and social factors and the changes that occur among these relationships over time [12]. A model and treatment approach that focuses on only one of these sets of factors will inevitably be incomplete and inadequate.

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SECTION 4

Pain Syndromes

CHAPTER 17

Myofascial Pain and Fibromyalgia Syndrome

Kathleen A. Sluka

Musculoskeletal pain conditions are common with regional pain complaints affecting up to 50% of the population and widespread pain complaints affecting up to 10% of the population [19,32]. One of the most common regional pain complaints is myofascial pain syndrome, which has been estimated to be the source of pain in 30% of the patients consulting primary care [69] and up to 85% of patients attending a pain center [24]. Fibromyalgia is one form of chronic widespread musculoskeletal pain that affects 4–12% of the population with females showing a greater prevalence than males [19,32,63]. It is less clear if there are sex differences in the prevalence of myofascial pain syndrome; some studies show a greater prevalence in females whereas others show no difference (Table 17-1) [32,63,68]. This chapter will review the diagnostic criteria and treatment strategies for people with myofascial pain syndromes and fibromyalgia, and general characteristics are outlined in Table 17-1.

MYOFASCIAL PAIN SYNDROME

Epidemiology and Diagnosis

Myofascial pain, historically, is considered a localized pain syndrome associated with trigger points in the muscle belly (Table 17-1). However, in some cases, myofascial pain has also been considered a regional pain syndrome of muscle origin, as in the case of myofascial pain from the temporomandibular joint. For the purposes of this chapter, myofascial pain will be considered as arising from trigger points in the muscle belly as described by Travell et al. [68]. It can be acute or chronic and has been recorded to affect approximately 20–30% of the population [63].

TABLE 17-1 **Characteristics of Myofascial Pain and Fibromyalgia**

Myofascial Pain (Trigger Points)	Fibromyalgia
Unclear female-to-male ratio	4–9:1 female-to-male ratio
Local or regional pain	Widespread, general pain
Local tenderness	Widespread tenderness
Trigger points	Tender points
Treatment with local therapy	Treatment with systemic therapy
Trigger point injection	Pharmacological therapy
Local stretching, strengthening	Cognitive-behavioral therapy
Ultrasound	Aerobic and strengthening exercise
TENS	TENS

Note: TENS, transcutaneous electrical nerve stimulation.

Distinct patterns of pain referral from trigger points have been identified in muscles across the entire body by Travell et al. [68]. Trigger points are particularly common in the upper cervical spine and shoulder region and can refer pain to areas of the head and face. However, there are trigger points in most muscles of the body including the limbs and lower back. Some examples of trigger points and their pattern of referral are shown in Fig. 17-1. There are distinct patterns with each trigger point, and adequately understanding and evaluating these patterns is critical to effective treatment.

There is limited consensus on diagnostic criteria for myofascial pain syndrome [79]. The four most common criteria used are tender spot in a taut band, patient pain recognition, predicted pain referral pattern, and a local twitch response. This chapter has adopted the criteria described by Travell et al. [68], which generally agree with that utilized in randomized controlled trials (RCTs) assessed by Tough et al. [79]. As stated by Travell et al. [68], the lack of consensus results in a serious impediment to well-controlled research to evaluate efficacy of treatments. For clinicians who treat myofascial pain, the two-volume series by Travell et al. [68] is essential to adequately diagnose and treat myofascial pain.

Diagnostic criteria as proposed by Travell et al. [68] are outlined in Table 17-2. In general, myofascial pain is a local or regional pain syndrome occurring in one or two body regions. Four essential criteria must be met to reach a diagnosis of myofascial pain: (1) There should be a palpable taut band in the muscle with (2) an exquisite spot tenderness of a nodule in the taut band. (3) The patient should recognize a current pain complaint by pressure on the tender nodule. This pressure should reproduce the clinical pain complaint and should not be associated with a new complaint. It should be recognized that *active* trigger points in a muscle reproduce the patient's pain complaints. *Latent* trigger points also exist, which have a taut band, spot tenderness, and referral of pain

but do not reproduce a clinical pain complaint. (4) The fourth essential criterion is restricted range of motion that is limited as a result of pain. Confirmatory observations include a local twitch response, either visual or on palpation, of the taut band. Although the twitch response is highly specific to myofascial pain syndromes, it is difficult to elicit reliably and has thus been considered a confirmatory observation. Relief of pain by stretching the muscle or trigger point injections also confirms myofascial pain syndrome.

TABLE 17-2 Diagnostic Criteria for Myofascial Pain and Fibromyalgia

Myofascial Pain (Trigger Points)	Fibromyalgia
Major criteria • Palpable taut band • Spot tenderness of nodule in taut band • Patient recognition of current pain complaint by pressure on nodule • Limited ROM with pain	Widespread, generalized pain: above and below midline; both sides of body, must include axial distribution Pain on digital palpation of 11/18 tender points Pain greater than 3-mo duration
Confirmatory criteria • Local twitch response on palpation • Pain in the distribution of expected trigger point in that muscle on compression of tender nodule • Pain alleviated by stretching muscle or injecting trigger point	

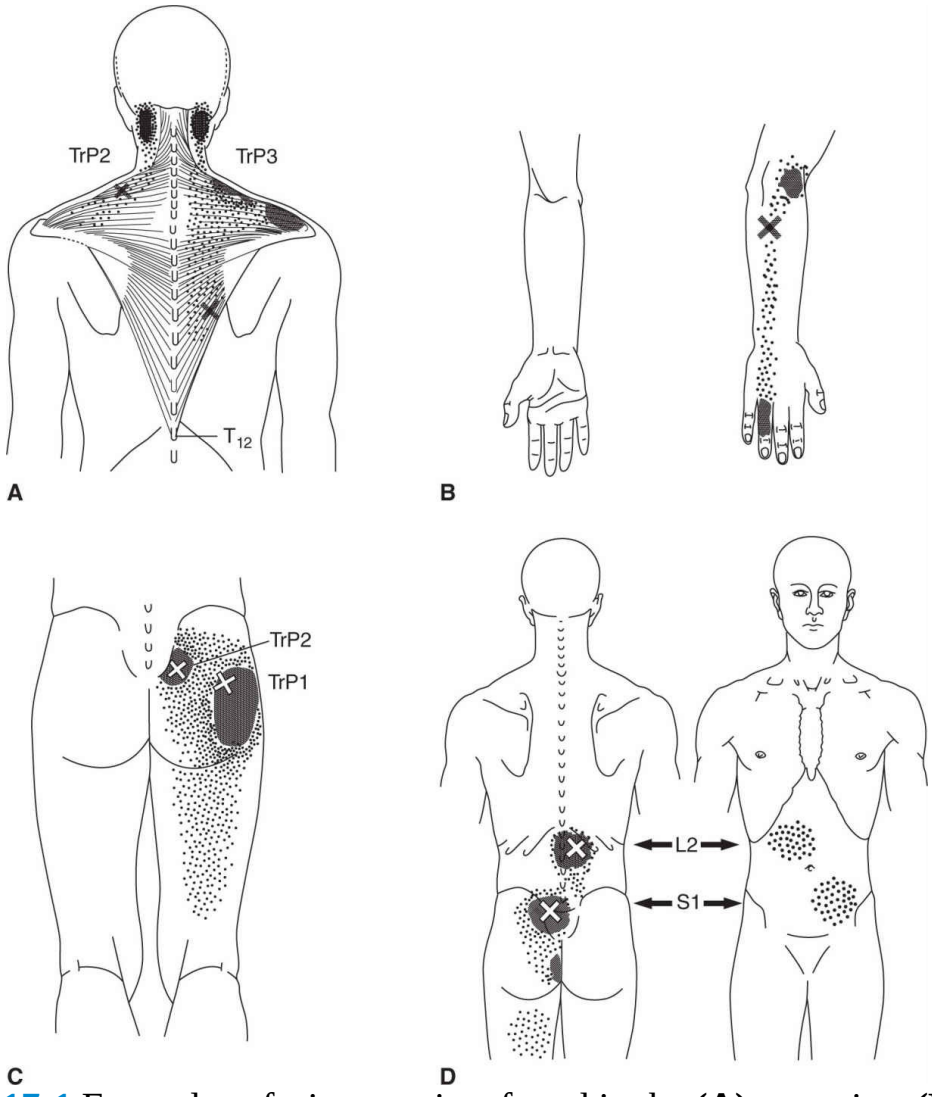


FIGURE 17-1 Examples of trigger points found in the **(A)** trapezius, **(B)** extensor digitorum of the forearm, **(C)** multifidus of the lower back, and the **(D)** piriformis. (Reprinted with permission from Travell et al. [68].)

Pathobiology

There is an increasing body of knowledge about the pathology of myofascial pain with recent studies focusing on myofascial trigger points [63,66]. There is evidence of increased muscle activity (end-plate noise) observed in active myofascial trigger points measured as end-plate noise [42], and spontaneous activity or end-plate spikes upon needle insertion into the active trigger points [61]. Ultrasound imaging of trigger points in muscle is able to distinguish active trigger points from normal tissue. These studies show a focal area of hypoechogenicity corresponding to the palpable nodule, suggesting denser

tissues [67]. Furthermore, muscles with active trigger points show changes in biochemical markers: increased substance P and calcitonin gene-related peptide (CGRP), bradykinin, interleukin-6, interleukin 1β, tumor necrosis factor-α, serotonin, and norepinephrine and decreased pH [64,65]. Interestingly these changes are located in muscles with active trigger points, but not those without trigger points, or those with latent trigger points. Thus, there are clear changes in muscle activity, and importantly in neurotransmitters, cytokines, and pH, which are known to activate and sensitize nociceptors. These changes may explain the underlying pain of myofascial pain syndrome and suggest peripheral mechanisms are important in the generation of myofacsial pain syndrome.

Assessment Considerations

Evaluation of people with myofascial pain syndrome should clearly utilize techniques to evaluate resting pain, pain during palpation of trigger points (e.g., pressure algometry), range of motion, and pain with active range of motion. In addition, the impact of the pain on the patient's overall functional capacity can be done with self-efficacy questionnaires or general quality-of-life surveys as outlined in Chapter 6. The therapist should employ a biopsychosocial approach to the assessment of myofascial pain that accounts for the multidimensional nature of pain and its impact on function and social roles, particularly for patients with chronic myofascial pain.

Medical Management

Treatment of myofascial pain syndrome from a medical perspective involves injection of trigger points. Injections can occur with botulism toxin, lidocaine, saline, or dry needling [13,20,23,26,70]. Trigger point injections typically decrease pain, increase pressure pain threshold, and increase range of motion in people with myofascial pain syndrome [13,23,26]. In fact, a recent systematic review shows strong evidence that dry needling decreases pain intensity and improves range of motion [13]. However, trigger point injections with lidocaine were superior to dry needling [48]. Furthermore, physiotherapy was more effective than dry needling [48].

There are few RCTs for treatment of myofascial pain with common pharmaceutical agents such as nonsteroidal anti-inflammatory drugs (NSAIDs), or antidepressants, and it is generally thought that treatment with trigger point injections followed by active physical therapy is the most effective one [63].

Cyclobenzaprine has been tested in those with myofascial pain in two small RCTs with conflicting results. One study showed improvement in pain intensity compared with placebo, and the other showed no significant differences when compared with lidocaine infiltration [46]. Recommendations for treatment of myofascial from the Professional Practice Committee of the Physical and Rehabilitation Medicine section of the Union of European Medical Specialists suggest beneficial evidence to support the use of ibuprofen (NSAID) along with sedatives (diazepam), and topical analgesics such as lidocaine, clonazepam, amitryptaline, or tropisetron. However, there is insufficient evidence for opioids, selective and nonselective reuptake inhibitors, or gabapentinoids [56].

Psychological Management

The use of psychological strategies for the treatment of myofascial pain syndrome has not been assessed in randomized controlled clinical trials. It is likely that with all chronic pain conditions the cognitive-behavioral therapy aimed at self-management and coping skills would be of great benefit. It is also highly likely that relaxation therapy and biofeedback could reduce any increased muscle activity in the trigger point as a result of myofascial pain.

Physical Therapy

Physical therapy interventions for myofascial pain generally involves multiple techniques including dry needling (see above), manual therapy, exercise, ultrasound, and transcutaneous electrical nerve stimulation (TENS). Passive stretching of the muscle with the trigger point is considered a primary treatment in people with myofascial pain syndrome. In an uncontrolled study, passive stretching along with fluoromethane spray decreased pain and increased pressure pain threshold [38]. Dry needling combined with active stretching exercises (as suggested by Simons et al. [68]) produced a greater reduction in pain when compared with patients doing active stretching alone, or a no-treatment control group [22].

Manual therapy generally uses trigger point massage or ischemic pressure application to the trigger point. Ischemic pressure has been applied in multiple RCTs and reduces pain intensity, increases in pain threshold, improves range of motion, and decreases disability [13,34,35,39,55]. When ischemic pressure is applied to the trigger point with active-range-of-motion exercises, there is reduced pain, increased pressure pain thresholds, and decreased amount of time

in pain during a 24-hour period greater than active-range-of-motion exercises alone. [35]. In fact, active-range-of-motion exercises alone have no effect on pain measures. Further, application of ischemic pressure in combination with trigger point injections (30–60 seconds) produces a greater reduction in pain intensity (decreased by 4 points vs. 2 points on a 10-point scale) and neck disability than trigger point injections alone [39].

The use of ultrasound is commonly used to treat myofascial pain. RCTs show mixed results; however, these are generally performed on a small sample of subjects. Continuous and pulsed ultrasound, as well as the placebo ultrasound, all show improvements in pain, severity of muscle spasms, and function; however, continuous ultrasound has greater improvement in pain at rest [37]. The use of conventional ultrasound (moved over the trigger point) when compared with placebo ultrasound gives no increased reduction in pain when combined with massage and exercise [27]. In this study, massage and exercise reduced the number and pain intensity of myofascial trigger points. However, Sberly and Dickey [71] show an increase in pressure pain thresholds in people with myofascial pain treated with conventional ultrasound (continuous, 1.0 W/cm^2, 5 minutes) but not with lower-intensity ultrasound (continuous, 0.1 W/cm^2, 5 minutes). Majlesi and Unalan [49] suggest better effectiveness with high-power pain threshold static ultrasound described as increasing the intensity to the level of maximum pain the subject could bear for 4–5 seconds and then reducing to 50% of this intensity for another 15 seconds, repeated three times. All subjects had acute myofascial pain and both groups performed active-range-of-motion exercises. Using this mode, and comparing with continuous 1.5 W/cm^2 for 5 minutes, over the trigger point, resulted in a significant reduction in pain and increase in ROM after the first treatment session that was substantially greater than conventional ultrasound. The number of visits required was significantly lower (2.8) when compared with the group that received conventional ultrasound (11.8). Both groups achieved the same end point of normal range of motion and pain at discharge on average between 1 and 2 points on the VAS. Unfortunately, there was no placebo control, or no untreated control to know if the conventional ultrasound group fared better than normal history or the use of active exercises alone. Comparing doses, higher doses of ultrasound (1.5 W/cm^2) or high-power pain threshold ultrasound showed greater improvements in pain intensity and pain thresholds when compared with placebo [40].

Effects of TENS on myofascial pain have been evaluated in several RCTs. Hsueh et al. [36] examined the effects of conventional TENS (sensory intensity,

60 Hz) and neuromuscular electrical stimulation (NMES) when compared with a placebo on pain, pressure pain threshold, and range of motion in people with myofascial pain syndromes. The studies showed that both TENS and NMES reduced pain and increased pressure pain thresholds with TENS having a greater effect on pain measures. NMES, however, also significantly increased range of motion, for which TENS had no effect. Using low-frequency TENS at motor contractions for 3 minutes, there was a reduction in pain and increase in pressure pain threshold in approximately 50% of subjects [52]. TENS is typically applied for longer durations and thus they may have had greater effects. However, a single treatment with low-frequency TENS applied at motor contraction for 10 minutes also had no effect on pain or pressure pain thresholds [31]. On the other hand, high-frequency TENS (100 Hz; pulse width of 50 or 250 μs) applied at a strong sensory intensity without motor contraction for 10 minutes reduced pain, but had no effect on pressure pain thresholds [31]. Low-intensity TENS, below 5 mA, had no effect on pain or pressure pain thresholds [31]. Burst-type TENS for 10 minutes to the upper trapezius showed significantly improved pain threshold when compared with placebo and cervical range of motion in people with latent myofascial trigger points [62]. In summary, high-frequency or burst TENS, at adequate intensity and duration, is effective for myofascial pain, and NMES has the greatest effects on range of motion.

Physical therapy usually combines multiple treatments to reduce myofascial pain. One study assessed the addition of combining multiple physical therapy treatments on myofascial trigger points by measuring pain threshold, pain tolerance, and subjective pain scores (VAS). The control group received hot packs with active range of motion and showed significant increases in pain threshold and tolerance and a small decrease in pain (0.77 points on a 10-point scale) [35]. Adding ischemic pressure or spray and stretch to the hot packs and active range-of-motion treatment showed similar increases in pain thresholds and tolerance but a greater decrease in pain (1.49 points on a 10-point scale). The addition of TENS or interferential therapy to the hot packs and active range of motion similarly increased pain threshold and tolerance and resulted in a further decrease in pain (2.23–3.64 points on a 10-point VAS scale). Addition of spray and stretch to the hot pack and active range of motion with ischemic pressure had no additional effect when compared with the group that received hot packs and active range of motion with ischemic pressure but without spray and stretch. Combined home exercise and self-massage with TENS and heat, when compared with passive treatments of heat and TENS alone, showed significant decreases in pain at rest and during activity, and both groups showed improvements in pain thresholds [17]. Thus, it appears that ischemic pressure of

the trigger point, applied by the therapist or the patient, reduces symptoms associated with myofascial pain, and addition of electrical nerve stimulation further decreases pain.

TABLE 17-3 **Summary of Efficacy for Myofascial Pain Treatments**

Treatment	Pain	Pressure Pain Threshold	Range of Motion
Trigger point injection	+ (RCT)	+ (RCT)	+ (RCT)
Active ROM exercise*	?	?	?
Ischemic pressure	+ (RCT)	+ (RCT)	+ (RCT)
TENS/interferential	+ (RCT)	+ (RCT)	– (RCT)
NMES	+ (RCT)	+ (RCT)	+ (RCT)
Conventional ultrasound	+ (RCT)	– (RCT)	– (RCT)
High-power, high-intensity ultrasound	+ (RCT)	+ (RCT)	+ (RCT)
Hot pack	– (RCT)	– (RCT)	– (RCT)
Spray and stretch	? Uncontrolled, RCT	? Uncontrolled, RCT	? Uncontrolled, RCT

*Usually used in combination with another therapy or as control group; generally not effective in isolation.

Abbreviations: +, positive effect; –, no effect; ?, unclear if effective but commonly utilized treatment; RCT, randomized controlled trial; TENS, transcutaneous electrical nerve stimulation; NMES, neuromuscular electrical stimulation.

At present there is little data to support the use of active-range-of-motion exercises alone for people with myofascial pain. Active exercises are given with the rationale of maintaining range of motion after treatments aimed at increasing that range of motion. There are no studies to date that performed treatments without the active exercise program, suggesting that inclusion of the active-range-of-motion exercises is the standard of care and is recommended [56]. Stretching exercises have not been systematically evaluated but a few studies show that there appears to be some effect of stretching alone or combined with trigger point therapy in reducing pain associated with myofascial pain syndrome. Efficacy for the various treatment options for myofascial pain syndrome is summarized in Table 17-3.

FIBROMYALGIA SYNDROME

Epidemiology and Diagnosis

Fibromyalgia syndrome is a generalized widespread pain condition with prevalence of 4–12% in the general population. It occurs primarily in women

(7:1 ratio) with a peak between 60 and 80 years of age [16]. People with fibromyalgia commonly present with sleep disorders (90%), fatigue (80%), depression (20–40%), irritable bowel syndrome (12%), and often have headache, cognitive deficits, chest wall pain, and morning stiffness [63]. It is, thus, distinctly different from myofascial pain, which is a localized pain condition without associated comorbidities.

Fibromyalgia syndrome classification was formalized in 1990 by the American College of Rheumatology [86]. These criteria are based on symptoms reported by the patient and found on physical exam. Specifically, there must be widespread pain for at least 3 months duration. The widespread pain is defined as occurring on both sides of the body and above and below the waistline and must include axial pain. On physical exam there should be 11 of 18 tender points to 4 kg of pressure applied by the clinician. These tender points are all bilateral and include occiput at the suboccipital muscle insertion site; low cervical at the anterior aspect of the intertransverse spaces of C5–C7; trapezius at the midpoint of the upper border; supraspinatus at the origins of the medial border of the scapular spine; second rib at the upper surfaces just lateral to the costochondral junctions; lateral epicondyle 2 cm distal to the epicondyles; gluteal in upper outer quadrant of buttock in the anterior fold of the muscle; greater trochanter posterior to the trochanteric prominences; and knee at the medial fat pad proximal to the joint line (Fig. 17-2, tender point picture). In 2010, an updated criterion was proposed to make diagnosis easier by eliminating the tender point exam [85]. A widespread pain index (WPI, 0–19 score) counts the number of areas in the body the person has had pain. A symptom severity scale (SS) requires a physician to rate severity on a 4-point scale for fatigue, waking unrefreshed, cognitive symptoms, and somatic symptoms. The person satisfies the criteria for fibromyalgia if the following three conditions are met: (1) WPI $\geq$7 and SS $\geq$5 or WPI 3–6 and SS $\geq$9, (2) symptoms present for at least 3 months, and (3) patient does not have a disorder that would explain the pain. It should be noted that with the newer criteria the female:male ratio is smaller and closer to 2:1 [18].

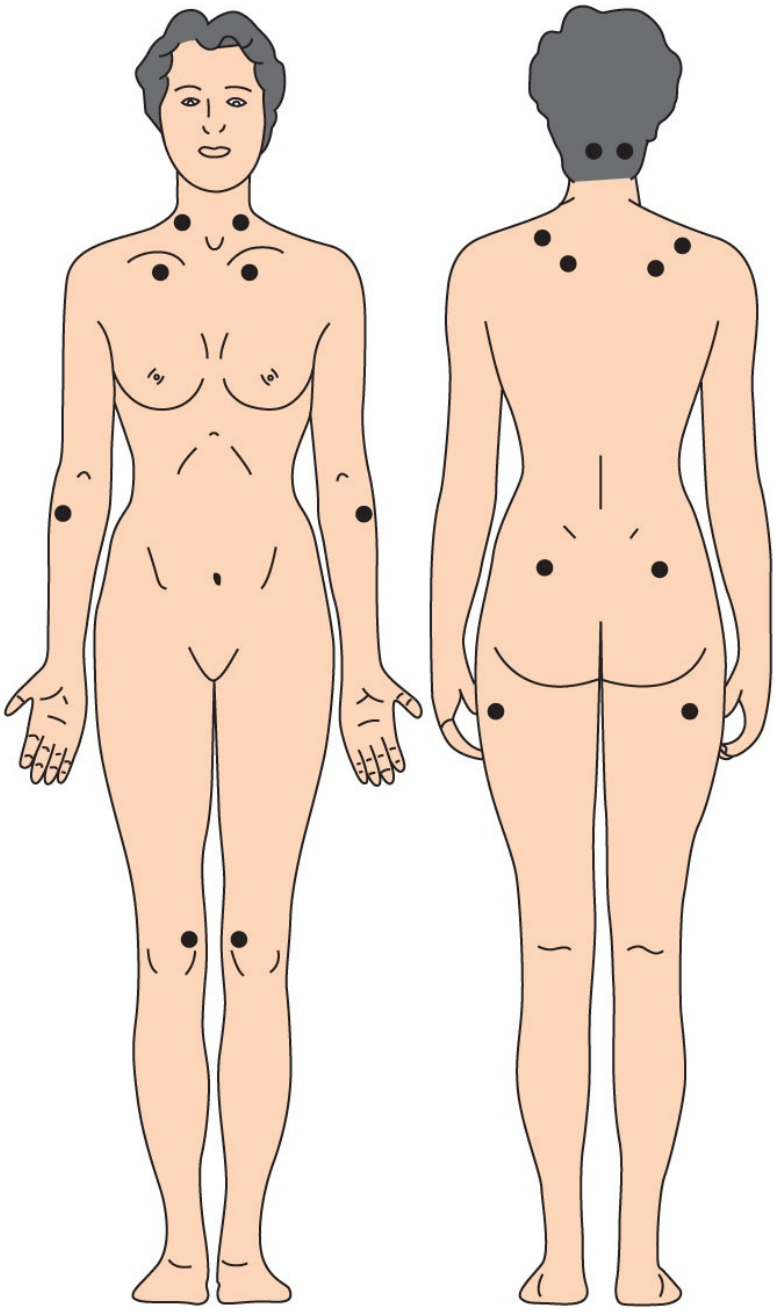


FIGURE 17-2 Diagram illustrating the tender point sites for diagnosis of fibromyalgia syndrome.

Pathobiology

Little is known about the etiology of fibromyalgia syndrome but it is commonly accepted that central sensitization underlies much of the pain complaints [18]. Fibromyalgia is, in its essence, a disorder of central pain amplification. Fibromyalgia patients interpret sensory afferent stimuli that would normally be

perceived as innocuous (or nonpainful) as noxious (or painful). It has now been clearly demonstrated in experimental settings that when a low-intensity stimulus is rated as painful by fibromyalgia patients, there is concomitant activation of brain regions receiving input from the spinothalamic tract known to be activated by painful stimulation [30]. Although the mechanism is not entirely known, is has become clear that fibromyalgia is associated with enhanced excitability in central pain transmission pathways [59,72,73,75,76] and loss of pain inhibition [41,44,45,74,76]. There are increases in substance P and nerve growth factor, and decreases in serotonin in the cerebrospinal fluid [63]. Importantly, centralization of the pain does not mean that there is not a peripheral nociceptive component to their pain that may be responsible for some of the pain. Rather, it means that the central nervous system responds in an exaggerated way to the incoming input. As proposed by Clauw, the individual's "set point" is modifiable by a number of factors including levels of neurotransmitters that facilitate pain and those that reduce pain. These changes may result in the comorbid symptoms like fatigue, cognitive dysfunction, disrupted sleep, and mood disturbances likely because they use the same neurotransmitters and pathways that control pain [18]. Together these data suggest that there is enhanced excitability in the central nervous system accompanied by decreased inhibition.

Although there is a general hypothesis that FM is a "central pain disorder," several reports show evidence of peripheral nerve abnormalities in people with FM. Specifically several studies report reduced numbers of epidermal nerve fibers in skin biopsies in people with FM compared with healthy controls [15,53,82]; these changes occur in approximately half of the fibromyalgia population. People with FM also had increased scores on neuropathic pain questionnaires, alterations in cold and warm detection thresholds measured by QST, and impaired pain-evoked responses [53,82]. Rice et al. [1] compared those with FM with healthy controls and show in skin biopsies over the hypothenar eminence there is an increased size and innervation of arteriole venule shunts. Using microneurography, Serra et al. [64] show that mechanically insensitive C fibers show enhanced spontaneous activity and sensitization to mechanical stimulation. Further injection of lidocaine into muscles of people with fibromyalgia significantly reduced local hyperalgesia at the site of injection and hyperalgesia outside the site of injection, and decreased pain by 38% [77]. Thus, peripheral factors may underlie some of the pain experienced by people with fibromyalgia. However, it is not clear if these factors are the primary cause or secondary to the condition itself.

Another theory for the pathology in FM suggests that chronic systemic inflammation drives the pain and associated symptoms of FM. In support, people

with FM show enhanced circulating inflammatory cytokines and enhanced release of inflammatory cytokines from circulating monocytes [6,7,28,57,58]. However, the literature on cytokines in FM is variable with some studies showing increases, some decreases, and some unchanged in circulating levels in the plasma or serum [51,78,80]. In a systematic review of the literature, Uceyler et al. [80] show increases in IL-1Ra, IL-6, and IL-8 in serum, and higher IL-8 in plasma. When using an isolated monocyte population, there is enhanced stimulated release of IL-β and TNFα in people with FM compared with controls [57]. When examining the relationship of cytokines to pain symptoms in FM, studies generally showed that increased cytokine levels correlate with increased pain scores and the FIQR (a disease-specific survey). Furthermore, Uceyler et al. [81] showed that reduced anti-inflammatory cytokines (IL-4 and IL-10) correlate with lower perceived levels of fatigue, and Caro and Winter [15] show a relationship between IL-2 receptor expression and nerve fiber density. Together these studies suggest that increases in the inflammatory cytokines IL-1β , IL-8, and TNFα are most consistently elevated in multiple studies in serum and in stimulated peripheral blood mononuclear cells or monocytes.

FIBROMYALGIA IMPACT QUESTIONNAIRE (FIQ)

Last name: **First name:** **Age:** **Today's date:**

Duration of FM symptoms (years): **Years since diagnosis of FM:**

Directions: For questions 1 through 11, please check the number that best describes how you did overall for the *past week*. If you don't normally do something that is asked, place an 'X' in the 'Not Applicable' box.

Were you able to:	Always	Most	Occasionally	Never	Not applicable
1. Do shopping?	☐0	☐1	☐2	☐3	☐4
2. Do laundry with a washer and dryer?	☐0	☐1	☐2	☐3	☐4
3. Prepare meals?	☐0	☐1	☐2	☐3	☐4
4. Wash dishes / cooking utensils by hand?	☐0	☐1	☐2	☐3	☐4
5. Vacuum a rug?	☐0	☐1	☐2	☐3	☐4
6. Make beds?	☐0	☐1	☐2	☐3	☐4
7. Walk several blocks?	☐0	☐1	☐2	☐3	☐4
8. Visit friends or relatives?	☐0	☐1	☐2	☐3	☐4
9. Do yard work?	☐0	☐1	☐2	☐3	☐4
10. Drive a car?	☐0	☐1	☐2	☐3	☐4
11. Climb stairs?	☐0	☐1	☐2	☐3	☐4
Subtotal scores *(for internal use only)*	☐	☐	☐	☐	☐
Total score *(for internal use only)*	☐				

12. Of the 7 days in the past week, how many days did you feel good?

☐0 ☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7

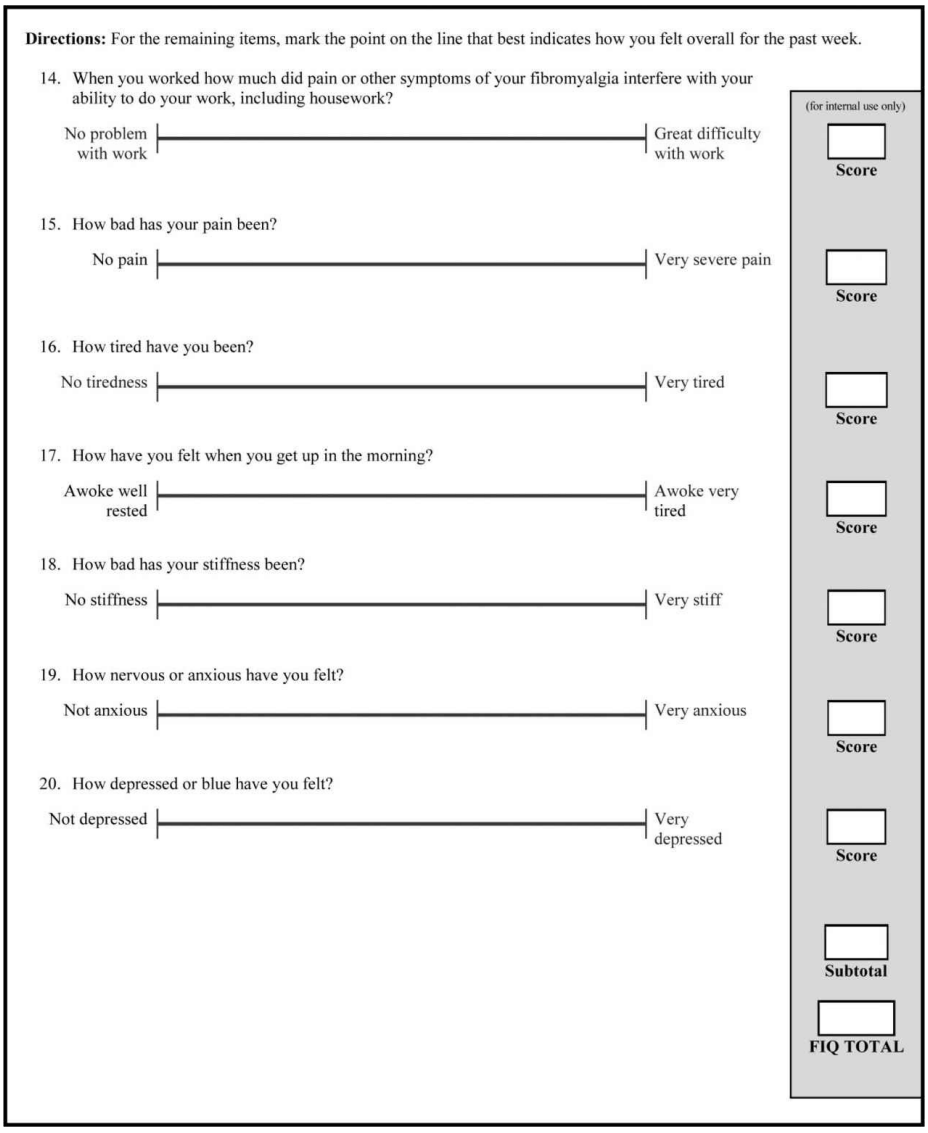
Score ☐

13. How many days last week did you miss work, including housework, because of fibromyalgia?

☐0 ☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7

Score ☐

(Continued)



Directions: For the remaining items, mark the point on the line that best indicates how you felt overall for the past week.

14. When you worked how much did pain or other symptoms of your fibromyalgia interfere with your ability to do your work, including housework?

No problem with work — Great difficulty with work

15. How bad has your pain been?

No pain — Very severe pain

16. How tired have you been?

No tiredness — Very tired

17. How have you felt when you get up in the morning?

Awoke well rested — Awoke very tired

18. How bad has your stiffness been?

No stiffness — Very stiff

19. How nervous or anxious have you felt?

Not anxious — Very anxious

20. How depressed or blue have you felt?

Not depressed — Very depressed

(for internal use only)

Score

Score

Score

Score

Score

Score

Score

Subtotal

FIQ TOTAL

FIGURE 17-3 Fibromyalgia Impact Questionnaire.

There appears to be a genetic link in some patients with fibromyalgia with female relatives more likely to develop fibromyalgia [12,18]. Studies show that up to two-thirds of mother, daughter, and sisters also have fibromyalgia. Genetic analysis of patients with fibromyalgia demonstrates polymorphisms of genes in the serotonergic, dopaminergic, and catecholaminergic systems [12,54].

Assessment Considerations

Evaluation of people with fibromyalgia must use a multidisciplinary approach to evaluate not only the pain, but also the impact of pain on function and quality of life. Patients with fibromyalgia should be referred to both physicians and psychologists, in addition to physical therapy, to receive an effective

multidisciplinary treatment. As a physical therapist, measurement of pain with standard subjective pain scales and the McGill Pain Questionnaire can give valuable information not only on the severity but also on the dimensions of pain. Quality-of-life surveys, self-efficacy questionnaires, fear avoidance surveys, and pain catastrophizing can give valuable information to the therapist on the impact of the pain on function, and the barriers to treatment with an active exercise program. The fibromyalgia impact questionnaire is a disease-specific questionnaire (Fig. 17-3) that takes 5 minutes to complete. This simple 20-question survey estimates the impact of fibromyalgia on activities of daily living and work, as well as fibromyalgia-associated symptoms such as fatigue, stiffness, depression, and anxiety [9]. It is useful not only for research but also in evaluating progress for patients with fibromyalgia.

Medical Management

Treatment of fibromyalgia syndrome requires a multidisciplinary approach involving pharmacological management, psychological treatments, and physical therapy (see Table 17-4 for a summary of the efficacy of various treatments). There is good evidence from RCTs that multidisciplinary treatment combining education, cognitive-behavioral therapy, and exercise was efficacious in patient self-efficacy, overall impact of the disease on quality of life as measured by the fibromyalgia impact questionnaire, decreasing pain, and improving function when compared with self-management strategies [18,25,29]. Treatment gains were maintained long term for up to 2 years [29]. Canadian Guidelines for the diagnosis and management of fibromyalgia, published in 2012, describe an evidence-based synthesis of recommended treatments [25] and are summarized in a recent review [18].

Pharmacological management is designed to reduce excitability or increase inhibitory neurotransmitters. Based on RCTs several drug classes show strong evidence for efficacy in fibromyalgia including tricyclic antidepressants (amitryptaline), gabapentinoids (gabapentin, pregabalin), and dual reuptake inhibitory (duloxetine, milnacipran) [18,25]. These drugs are effective for reduction in pain, improvement of sleep, decreasing fatigue, and improving improving overall well-being, supported by meta-analysis of existing literature and recommended in clinical evidence-based guidelines [3,18,25,29,50,60]. However, NSAIDs and opioids are not efficacious in treating people with fibromyalgia [18,25,60].

TABLE 17-4 **Treatment of Fibromyalgia Syndrome**

Treatment	Details	Evidence Level
Nonpharmacological Therapies		
Patient education	Self-management principles	Strong
Exercise	Aerobic and strengthening exercises effective	Strong
Cognitive-behavioral therapy	Effective in one-on-one setting, small groups and Internet based	Strong
TENS [14,21,43]	Emerging evidence from recent randomized clinical trials	Moderate
Massage therapy [47]	Recent systematic review of nine trials	Strong
Pharmacological Therapies		
Tricyclic antidepressants	Amitriptyline and cyclobenzaprine	Strong
Dual reuptake inhibitors	Serotonin and norepinephrine reuptake inhibitors, duloxetine and milnacipran	Strong
Gabapentinoids	Gabapentin and pregabalin	Strong
γ-hydroxybutyrate	Used for treating narcolepsy and cataplexy	Strong
Selectric serotonin reuptake inhibitors	Fluoxetine, sertraline, paroxetine	Strong
Nonsteroidal anti-inflammatory drugs	No evidence of efficacy	No evidence
Opioids	Tramadol with or without acetominophin	No evidence

Source: Adapted from Clauw [18], Fitzcharles et al. [25], and Goldenberg et al. [29] unless noted.

Psychological Management

Psychological management of fibromyalgia involves the use of cognitive-behavioral therapy, relaxation exercises, and instruction in coping skills. Strong evidence to support the effectiveness of cognitive-behavioral therapies for reducing pain and improving quality of life in individuals with fibromyalgia has been confirmed in systematic reviews and clinical practice guidelines [18,25,63]. Stress management and relaxation therapy also reduce pain in people with fibromyalgia [83]. In fact, adding cognitive-behavioral therapy to a standard medical care program of exercise and pharmacotherapy provides a sustained improvement in physical functioning [84].

Physical Therapy

Physical therapy should emphasize an active protocol aimed primarily at exercise and in particular aerobic conditioning programs. There is strong support for the use of aerobic cardiovascular exercise, moderate evidence for

strengthening exercises, and weak evidence for aquatic exercises in the treatment of fibromyalgia [4,5,10,11]. In a recent review of systematic reviews, Bidonde et al. [4] noted 9 systematic reviews comprising 60 RCTs and 3816 participants that used a diversity of exercise interventions. Although dosing recommendations were unclear in this review, there is moderate-quality evidence that aerobic-only exercise training at intensity levels recommended by the American College of Sports Medicine has positive effects on pain, global well-being, and physical function. Strengthening exercises (21 weeks), as recommended by the American College of Sports Medicine, also show improvements in pain as well as global well-being, tender points, and possibly depression. In several studies, improvements in pain, fibromyalgia impact questionnaire, function, and depression were maintained long term, 6 months to 2 years, following aerobic exercise. Overall, these studies show decreases in pain and increases in quality of life, and one study also shows a decrease in fatigue and improvement in depression [2,5,10,11,33].

Other physical therapy interventions including massage and electrotherapy may have some benefit. A recent systematic review examined effects of massage therapy for those with fibromyalgia and included 9 RCTs with 404 subjects. They show that massage therapy for >5 weeks significantly improved pain, anxiety, and depression, but not sleep disturbances [47]. These effects are immediate and there is no evidence of effectiveness for long-term follow-up [8,47]. TENS has recently been studied in those with fibromyalgia. When electrodes are placed over the spine, there is a reduction in pain, increase in pain threshold, and reduction in analgesic consumption [14,21,43]. Interestingly, TENS also restored conditioned pain modulation in subjects with fibromyalgia and increased pain thresholds outside the site of stimulation, suggesting a normalization of pain responses [21]. Thus, physical modalities such as massage and TENS may be useful adjuncts to help patients manage the pain associated with fibromyalgia. They may be useful to reduce pain in order for someone to better perform their exercise program.

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CHAPTER 18

Temporomandibular Disorders and Headache

Kathleen A. Sluka

Disorders of the head and face include temporomandibular joint disorder (TMD) and headache. Headache is the most common pain problem with tension-type headaches showing a prevalence of 30–78% while that of migraine is 10–12% [34,69]. The international classification of headache disorders supports three classifications of headache: migraine, tension-type headache and cluster headache, and other trigeminal autonomic neuralgias [39]. Although these types of headaches are defined and described separately, it should be kept in mind that many people with headaches have a mixture of migraine and tension-type headache. TMDs involve pain around the temporomandibular joint (TMJ) and muscles that control jaw movement. TMD conditions fall into three main categories: myofascial, internal derangement of the joint, and arthritis. Many people with TMD also have tension-type headaches and there is often a mixture of two or three of the TMD conditions in one patient. As with other chronic pain conditions, migraine, tension-type headache, and TMD are more common in women than men.

MIGRAINE

Epidemiology and Diagnosis

Migraine headaches are episodic with recurrent attacks lasting from 4 to 72 hours, are typically unilateral in adults, and usually located in the frontotemporal region of the head [34]. The headache is characterized by sensitivity to normal sensory input such as light, sound, touch, and head movement. After the attack the patient is commonly fatigued. Classically, migraine is associated with an aura, which consists of visual, sensory, or auditory disturbances that usually precede the headache. However, migraine without aura is more common than

migraine with aura occurring in a ratio of 2:1. Like many pain conditions, there are more females than males (male:female 1:2–3) afflicted with migraine [66]. Interestingly, migraine can start very early in life affecting approximately 7% of children, and the prevalence increases with age [45]. In a survey of the German population the mean age of onset was 7 with some reporting age of onset in the range of 1–3 years [45]. The majority of people with migraine have infrequent attacks (one per month); however, about 20% of people with migraine have more than one attack per month [66]. Diagnostic criteria for migraine with and without aura are outlined in Table 18-1 [39].

TABLE 18-1 Diagnostic Criteria for Migraine with and without Aura [40]

A. Five attacks (WITHOUT AURA) or two attacks (WITH AURA)

B. Headache lasting 4–72 h (WITHOUT AURA)

C. Headache with two of the following: unilateral, pulsatory, moderate to severe pain, aggravated by routine physical activity (i.e., walking)

D. During headache one of the following: (1) nausea or vomiting; (2) photophobia or phonophobia

E. Not related to other diseases

F. Fully reversible visual, sensory, or speech symptoms (no motor weakness) (WITH AURA)

G. At least two of the following: (1) visual (i.e., flickering lights, spots or loss of vision), sensory (i.e., pins and needles, numbness) symptoms, dysphagic speech disturbance; (2) one symptom gradually develops over 5 min, or (3) symptoms last between 5 and 60 min

Pathobiology

The pathobiology of migraine is likely multifactorial involving both peripheral and central mechanisms (for review see references [22,63]). Migraine is considered a neurovascular disorder. The blood vessels supplying the brain and dura mater are innervated largely by unmeylinated C-fibers [22,33,59,63]. Further, the connective tissue surrounding the brain, pia, arachnoid, and dura is also innervated by nociceptors [63]. Release of neuropeptides, such as substance P and calcitonin gene-related peptide, from the peripheral terminals of nociceptors causes vasodilation, with subsequent sensitization of nociceptors and sensitization of central neurons in the trigeminal system [33,63].

Migraine aura has been associated with cortical spreading depression, and a slow-propagating wave of neuronal and glial depolarization followed by a prolonged inhibition of cortical activity [63]. The depolarization is associated with release of neurochemicals that diffuse to the cortical surface to activate nociceptors innervating the pia to trigger neurogenic inflammation [63]. Further, functional neuroimaging studies suggest that activation of midbrain and

brainstem regions plays a critical role during migraine attacks [22,34]. Alterations in the serotonin system also appear to play a role in migraine. Specifically, it is thought that there is depletion in serotonin centrally that contributes to sensitization, and that there is an increase in the serotonin transporter in patients with migraine [37,71]. Genetic polymorphisms in the 5-HT transporter gene are also observed in migraine and have been linked to the frequency of attacks, and susceptibility or predisposition to migraine [37]. One form of migraine has a genetic link. Familial hemiplegic migraine (FHM) is a rare form of migraine (0.01% prevalence) that runs in families and results from mutations in one of the following genes: $Ca_v2.1$, a subunit of the P/Q voltage-gated calcium channel (50% of FHM); ATP1A2, which encodes the α2 subunit of the Na^+/K^+ pump; and SCN1A, which encodes a voltage-gated sodium channel [34]. In summary, migraine likely depends on activation of the trigeminovascular pathways with nociceptive signals originating in peripheral nociceptors and on dysfunction of central nervous system sites involved in neuronal excitability and pain.

Assessment Considerations

Assessment of pain in people with migraine should include not only the severity of the pain, but also the frequency of the headache. In addition, the impact of the migraine on quality of life and disability resulting from the migraine should be assessed. Risk factors for development of chronic migraine should also be addressed and include obesity, history of frequent headache, caffeine consumption, and overuse of as-needed medications [78]. The Migraine Disability Assessment Scale is a simple scale that is validated and easy to use (see Table 18-2) [79]. On the basis of the total number of days in questions 1–5, the following graded definition can be given to the patient for disability: I, minimal or infrequent disability, score = 0–5; II, mild or infrequent disability, score = 6–10; III, moderate disability, score = 11–20; IV, severe disability, score = 21+.

TABLE 18-2 Migraine Disability Assessment Scale

Instructions: Please answer the following questions about ALL your headaches you have had over the last 3 months. Write your answer in the box next to each question. Write zero if you did not do the activity in the last 3 months

1. On how many days in the last 3 months did you miss work or school because of your headaches? ____days
2. How many days in the last 3 months was your productivity at work or school reduced by half or more because of your headaches (not including days in 1) ____days
3. On how many days in the last 3 months did you not do household work because of your headaches ____days
4. How many days in the last 3 months was your productivity in household work reduced by half or more because of your headaches (Do not include days in 3) ____days
5. On how many days in the last 3 months did you miss family, social, or leisure activities because of your headaches? ____days

A. On how many days in the last 3 months did you have a headache (if a headache lasted more than one day count each day) ____days

B. On a scale of 0–10, on average how painful were these headaches? (0 = no pain; 10 = worst pain imaginable) _____

Medical Management

Treatment of migraine is primarily managed with pharmacological agents either designed to treat the acute attack or designed to prevent the frequency of attack. Guidelines for management of migraine have recently been published by the American Academy of Neurology [42,74]. Patients are also frequently taught nonpharmacological techniques to assist in management of the migraines [34]. These nonpharmacological treatments include education on how to avoid triggers, relaxation therapy, and biofeedback. Pharmacological and nonpharmacological treatments aimed at managing migraines generally will reduce the frequency of attack, but not the intensity of the pain during an attack. On the other hand, pharmacological agents aimed at treating the acute attack will reduce the intensity of the pain. The most effective treatment for acute attacks is the use of triptans, the most common of which is sumitriptan with efficacy confirmed in systematic reviews [16–19]. These are vasoconstrictors, which are 5-HT1B/1D agonists and are aimed at treating the pathology. Prophylactic treatments include long-term use of β-blockers, anticonvulsants, antidepressants, serotonin antagonists, and calcium-channel blockers [22,34]. Systematic reviews show that use of β-blockers and anticonvulsant drugs reduces the frequency of migraine attacks [11,46–48]. Thus, there is good evidence that the intensity and duration of the headache of an acute attack are effectively treated with sumitriptan, and that prophylactic treatments with β-blockers and anticonvulsant drugs reduce the frequency of attacks.

Psychological Management

Nonpharmacological approaches that include relaxation, biofeedback, or other psychological approaches such as cognitive-behavioral therapies have only been minimally studied. Systematic reviews show limited evidence of headache improvement with relaxation therapy when compared with wait-list controls, and no evidence for effectiveness of biofeedback when administered in isolation [13]. Combining nonpharmacological approaches results in improvements in headache symptoms when compared with wait-list controls with moderate evidence for an effect of relaxation and biofeedback and limited evidence for an effect of relaxation with cognitive-behavioral therapy compared with placebo [13,50].

Physical Therapy

The use of physical therapy aimed at improvement in posture, cervical range of motion (ROM), and strength is essentially ineffective in the treatment of migraine. However, if physical therapy is given to subjects after they are unresponsive to relaxation and biofeedback techniques, there is a much greater improvement [50]. Further, according to systematic reviews, spinal manipulation or mobilization of the cervical spine, delivered by a chiropractor or a physiotherapist, reduces frequency, severity, and disability [6]. However, this is based on weak evidence and not recommended in practice guidelines [6]. In a large population-based study, there is an increased risk and greater frequency of migraine headaches with low physical activity levels [83]. A randomized controlled trial (RCT) compared a 12-week exercise program with relaxation therapy and topiramate and showed a significant and equivalent decrease in headache frequency in all three groups [82]. Thus, physical therapy on its own is not effective for treatment of migraine, but may be effective as an adjunct therapy if combined with relaxation and biofeedback treatments. Further exercise therapy may be helpful in the reduction of the frequency of migraine headaches.

CLUSTER HEADACHE

Cluster headaches occur in the orbital, supraorbital, or temporal areas and are associated with excruciating pain [33]. The headaches are very frequent

occurring between 0.5 and eight times per day and are short-lived lasting between 30 and 180 minutes. The headache is accompanied by at least one of the following symptoms: lacrimation, nasal congestion or rhinorrhoea, eyelid edema, forehead and facial swelling, meiosis and/or ptosis, and a sense of restlessness or agitation. The incidence of cluster headache is very rare occurring in 0.1–0.4% of the population with men affected greater than women. The pain associated with cluster headache is typically described as sharp, boring, drilling, stabbing, or piercing, but not throbbing like migraine. The pain is excruciating and typically leaves the person exhausted for some time after the attack. Medical management is essential and physical therapy is generally not thought to be effective.

TENSION-TYPE HEADACHE

Epidemiology and Diagnosis

Episodic tension-type headaches can be difficult to distinguish from migraine without aura. The lifetime prevalence of tension-type headache is 79% and females are more likely to develop tension-type headaches than males [69]. Tension-type headaches commonly have a muscular component (associated with pericranial tenderness) with tenderness to palpation of the cranium typically at the base of the skull and around the temporal region (Fig. 18-1).

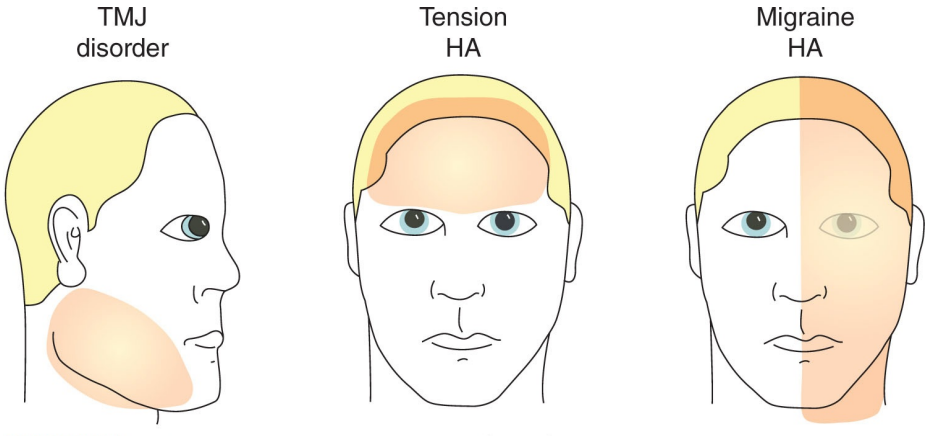

FIGURE 18-1 Schematic diagram showing areas of pain for people with migraine, tension-type headache, and TMDs. TMJ, temporomandibular joint; TMDs, temporomandibular joint disorders.

Diagnostic criteria for tension-type headache by the International Headache

Society in 1988 are utilized widely for diagnosis and for research [39]. Tension-type headaches can be classified as episodic occurring with a frequency of less than 15/mo or chronic occurring with a frequency of greater than 15/mo [69]. Episodic tension-type headache has been subdivided into infrequent (less than 1 d/mo) and frequent (1–14 d/mo). These headaches can be further subclassified as those associated with pericranial tenderness and those without. Diagnostic criteria for tension-type headache are outlined in Table 18-3 [39].

Pathobiology

There is little data on the underlying pathology associated with tension-type headaches. The pathobiology of tension-type headache has been previously reviewed and is summarized [69]. However, electromyographic (EMG) activity in the pericranial muscles is higher in people with tension-type headaches and bears a positive correlation with the intensity of the headache [70]. Further, there is increased cervical muscle co-contraction during cervical flexion and extension [29]. There are decreases in pressure pain thresholds in the pericranial area, as well as sites distinct from this area such as the hands or lower leg [70]. People with chronic tension-type headaches also have a greater number of active trigger points and greater pain intensity on palpation of the trigger points [12]. A number of neurochemicals have been explored. Nitric oxide (NO) can induce a headache in those with tension-type headache similar to that experienced by the subject [69]. Platelet levels of serotonin are elevated, and plasma catecholamine (epinephrine, norepinephrine, dopamine) levels are decreased in those with tension-type headache. A positive correlation occurs between dopamine and duration of history of headache and a negative correlation occurs between epinephrine and severity of headache [8]. Schoenen and Sava [69] propose that there is an interaction between alterations in central processing of nociception and the peripheral nociceptors. Physical stressors promote increases in muscle tension and emotional stressors can alter central activity to result in the headache [69]. Together these data suggest that there may be local changes that result in peripheral sensitization that leads to alterations in central neuron processing of nociceptive stimuli and central sensitization.

TABLE 18-3 **Diagnostic Criteria for Tension-Type Headache [40]**

A. Episodic: less than 15 headaches/mo; Chronic: greater than 15 headaches/mo

B. Headache lasting from 30 min to 7 d

C. At least two of the following: (1) pressing or tightening quality; (2) mild or moderate intensity; (3) bilateral; (4) not aggravated by routing physical activity

D. Both of the following: (1) no nausea or vomiting; (2) photophobia and phonophobia are absent but may have one of the two

E. Not attributed to another disorder

F. Subtypes: associated with pericranial tenderness or not associated with pericranial tenderness

Assessment Considerations

Assessment of tension-type headache should include standard pain measures, such as pain intensity ratings and the McGill Pain Questionnaire. In addition, assessments of self-efficacy and quality of life should also be considered as there can be significant impact on daily function in this group of patients. Further, understanding the frequency of headaches, the duration of each headache, and the intensity of headaches is important in examining and assessing the impact of treatment. Palpation for tenderness over muscle groups will help guide manual therapy treatments.

Medical Management

The first choice of pharmacological treatment for tension-type headaches is the NSAIDs and this class of drugs reduces the intensity of the headache and is recommended in clinical guidelines produced by the European Federation of Neurological Societies (EFNS) [5,69]. If NSAIDs are ineffective, or patients have chronic tension-type headaches, tricyclic antidepressants are a common prophylactic pharmacological therapy [69]. Systematic reviews, however, do not support the use of SSRIs for prophylactic treatment of tension-type headache [55] and there is little evidence for pharmacological therapy in tension-type headache [69].

Psychological Management

Nonpharmacological treatments include relaxation therapy, biofeedback, cognitive-behavioral therapy, and physical therapy. There is good evidence that psychological therapies such as relaxation therapy and biofeedback are effective for tension-type headache and are recommended by the EFNS [5,26,27]. Although cognitive-behavioral therapy is recommended in these guidelines for

tension-type headache, the evidence is limited [5].

Physical Therapy Management

Physical therapy is typically not effective for people with cluster or migraine headaches. However, tension-type headaches of muscular origin are effectively treated with physical therapy. Physical therapy for people with tension-type headache typically involves education regarding posture and biomechanics, and an exercise program aimed at improving posture of the cervical spine. Manual therapy is also commonly utilized to reduce muscle contraction in the upper cervical spine and the temporalis muscles, and to reduce pain. Massage, mobilization, or manipulation is also commonly utilized and effective in treating tension-type headache [28]. In a systematic review on spinal manipulation for tension-type headaches, Posadzki and Ernst [65] suggest that four out of five trials show greater effectiveness than their comparator group (sham/placebo, usual care, no intervention) but were unable to make conclusions. In a systematic review, manual therapies were more effective than no treatment at reducing headache frequency and intensity [9]; however, there were no placebo comparisons. Similarly, a meta-analysis examining effectiveness of manual therapies compared with pharmacological therapies in treatment of tension-type headache showed that manual therapies were more effective for reducing headache frequency, intensity, and duration immediately after treatment, but there were no differences in long-term follow-up [53]. When trigger point–focused massage was compared with placebo for tension-type headaches in a more recent clinical trial, there was no difference in HA frequency, intensity, or duration between active and placebo groups, but there were increases in pressure pain thresholds, and patient-reported perceived clinical change was greater for the active over placebo [58]. The use of other pain-relieving modalities, that is, transcutaneous electrical nerve stimulation (TENS), heat, or cold, is unclear and has not been studied in RCTs. However, as they are easy to use, inexpensive, and have negligible side effects, they should be tried to reduce pain and muscle tension.

There is limited research to support the use of physical therapy in tension-type headache. However, evidence from RCTs is generally favorable. Torelli et al. [81] examined the effect of 8 weeks of physical therapy on people with tension-type headache and compared with a group that received an 8-week observation period by a neurologist which then received physical therapy. The physical therapy group consisted of treatment two times per week for 4 weeks of massage, relaxation, stretching, and a home exercise program. The last 4 weeks

consisted of an exercise program only. The main measurement outcome was headache frequency and the goal of treatment was to instruct the subjects to manage the condition on their own. In both episodic and chronic tension-type headache, the frequency of headache and consumption of analgesics was reduced with physical therapy treatment after 8 weeks and maintained at a 12-week follow-up period with the effect greater in the chronic tension-type headache patients. Intensity and duration of the headache were unaffected by physical therapy treatment. Similarly, Hammill et al. [38] show a reduction in the frequency of headache, and an improvement in the sickness impact profile, a quality-of-life measure, with a physical therapy treatment consisting of education for posture at home and workplace, isotonic home exercise, massage, and stretching to the cervical spine muscles. A long-term follow-up at 12 months showed this effect continued through the follow-up period. Therefore, a multimodal approach to physical therapy aimed at education, exercise, and manual therapy is likely the most effective physical therapy approach for people with tension-type headaches.

TEMPOROMANDIBULAR DISORDERS

Epidemiology and Diagnosis

TMDs involve pain and dysfunction around the TMJ and muscles that control jaw movement [32,62]. TMD is more common in women and incidence rates vary but are somewhere between 3% and 15% of the population with a greater incidence in females [32]. Recent incidence rates of new onset TMD from the OPPERA study show a per-annum incidence of 3.9% and females only have a slightly greater incidence rate than males [76]. Interestingly, one-quarter of people with first-onset TMD stated that symptoms began as headache and not jaw pain [76]. TMD conditions fall into three main categories: myofascial pain, internal derangement, and arthritis [32,62]. Myofascial pain involves pain in the muscles that control jaw function. Myofascial pain associated with TMD is a general term used to describe pain associated with muscle and does not necessarily include trigger points as defined for myofascial pain below the head [32,62].

TMD can be acute, is generally cyclical, and usually goes away with little or no treatment. In some conditions, however, the pain can become chronic and result in significant disability and loss of function [32,62]. Pain is generally

worse with function and there is tenderness over the muscles surrounding the jaw and neck [32,62]. The pain is poorly localized, a dull aching pain, and bilateral. It is often referred to the ear, mandible, and temporal areas but can also be located in the teeth and face [32,62] (Fig. 18-1). There is decreased function of the jaw measured as a decrease in bite force, limited jaw opening, and asymmetrical mandibular movement [32,62]. Headache is also commonly associated with TMD, and there is a higher incidence of tension-type headache (but not migraine) in people with TMD. EMG analysis of the masticatory muscles shows hyperactivity, and an asymmetrical recruitment of the temporal and masseter muscles (which are normally symmetrical).

Internal derangement of the TMJ is thought to be an abnormal relationship between the articular disc and the mandible, fossa, and articular eminence [61]. Symptoms include pain, limited mouth opening, deviation of mouth opening, and clicking, cracking, or snapping when opening the jaw. Diagnosis is typically made by magnetic resonance imaging, along with assessment of signs and symptoms. The etiology of internal derangement is thought to be a result of trauma, muscle hyperactivity, or hyperextension of the mandible. Arthritis, either osteoarthritis and rheumatoid arthritis, can occur at the TMJ joint and result in similar conditions to that outlined in Chapter 22.

Pathobiology

Data from animal and human studies suggest that there are alterations in the peripheral and central nervous systems in TMD [7,32]. Myofascial pain of the muscles of mastication, and arthritis of the TMJ, are forms of chronic musculoskeletal pain with similar underlying mechanisms to those associated with the spine or extremities [32]. Inflammation of the masticatory muscles, or the TMJ, results in peripheral and central sensitization including changes in brainstem facilitatory and inhibitory pathways [7,72]. These changes likely underlie the pain and hyperalgesia observed in people with TMD [72].

The National Institute of Dental and Craniofacial Research (NIDCR) has funded a clinical study since 2006 called Orofacial Pain: Prospective Evaluation and Risk Assessment (OPPERA). This unique prospective study followed pain-free volunteers across a minimum of 3 years to identify biopsychosocial and genetic risk factors in the development of TMD. This study has produced an enormous amount of data identifying biopsychosocial risk factors that contribute to the onset and persistence of TMD. Importantly, this is the first study to examine for causal effects. The findings are summarized in a series of papers in a special issue of the Journal of Pain in 2013 [30,36,64,68,75,77] with an

overview given by Slade et al. [76]. To summarize, a number of potential risk factors for first-onset TMD were identified with older age, African American, pain on jaw opening and palpation tenderness of head and neck muscles, increased incidence of other regional pain conditions (i.e., low back pain, irritable bowel syndrome, etc.), other nonspecific comorbid conditions (e.g., fibromyalgia, depression), and lower overall quality of life and health status. Surprisingly, although there was an association between quantitative sensory testing measures such as pressure pain thresholds, these were weak associations. Psychological variables were also predictors of first-onset TMD with the strongest being higher somatic awareness followed by anxiety and perceived stress. The authors suggest that the psychological variables, measured in pain-free individuals, influence the development of TMD rather than develop as a consequence of chronic painful TMD.

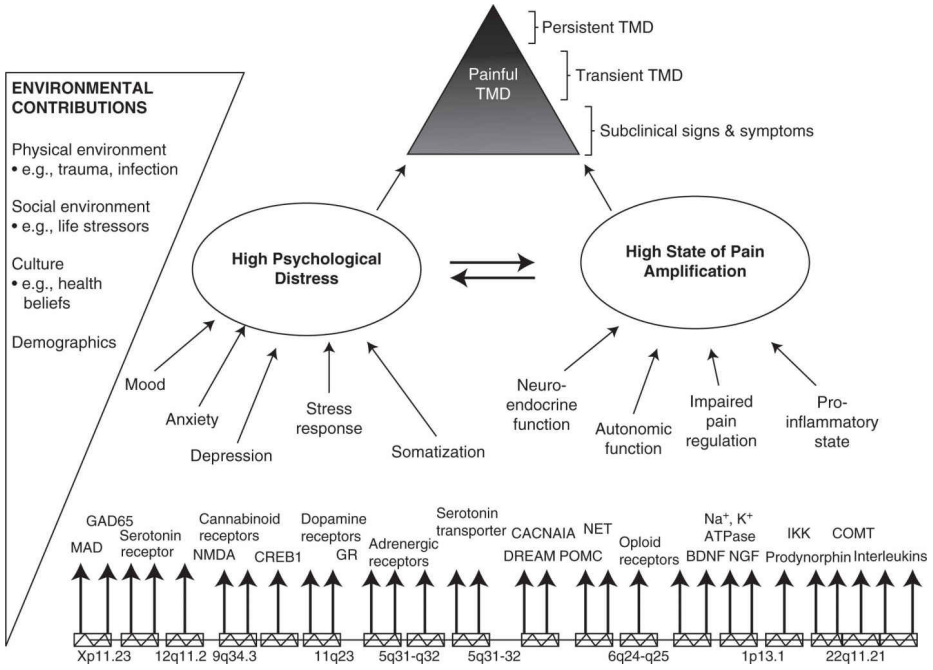

FIGURE 18-2 Summary of risk factors for development of TMD (temporomandibular joint disorder). Two phenotypes high psychological distress and high pain amplification could contribute to the onset and persistence of TMD. Multiple risk factors could contribute to these phenotypes. The risk factors are modulated and subject to genetic regulation as well as modified by environmental factors. (Reprinted with permission from Slade et al. [76].)

Lastly, the study examined genetic predictors and identified several single-nucleotide polymorphisms (SNPs) in specific genes that were associated with different symptoms: (1) nonspecific orofacial symptoms were associated with

SNPs in a sodium channel and the angiotensin enzyme, (2) global psychological and somatic symptoms were associated with an SNP in a gene encoding an enzyme that catalyzes the conversion of arachidonic acid to prostaglandin, and (3) negative affect and stress were associated with an SNP in the gene encoding an amyloid precursor protein [77]. Prior studies by this group show that polymorphisms in the catecholamine-*O*-methyltransferase (COMT) and β2-adrenergic receptor underlie the susceptibility to development of TMD [20,21], which is associated with the catecholamine pathway. In normal subjects, there are three major COMT haplotypes (LPS, APS, and HPS) that determine COMT enzymatic activity [20]. The LPS haplotype is associated with low pain sensitivity, APS is associated with higher pain sensitivity, and HPS with the highest pain sensitivity. In those individuals who developed TMD, there was a higher incidence of the HPS haplotype of the COMT gene. There was also an increased incidence for development of TMD in individuals with a genetic polymorphism in the β2-adrenergic receptor that would associate with high expression of the receptor. Thus, alterations in multiple genes may influence the development of TMD.

From these studies, the group has developed a model with two principal phenotypes, psychological distress and pain amplification, which contribute to the onset and persistence of TMD. Each phenotype consists of several specific risk factors, all of which are subject to genetic and environmental influences. Fig. 18-2 shows this model.

Assessment Considerations

As with all pain conditions, particularly those that are chronic, adequate assessment of pain using subjective pain measures is essential. In addition, ROM of the jaw (jaw opening distance) should be measured in all subjects. Assessment of pain's impact on function and quality of life is also valuable to develop a treatment plan and to assess the plan's success. Lastly, potential psychosocial factors that may interfere with success should be assessed.

Medical Management

Treatment of people with TMJ varies depending on the underlying problems. Therapy generally involves pharmacological management, self-care management, cognitive-behavioral therapy, physical therapy, and splint therapy. In some cases, particularly for internal derangement of the TMJ, arthroscopic

surgery is used.

Few studies have assessed the effectiveness of current pharmacological treatment for chronic TMDs and orofacial pain. Commonly used therapies include NSAIDs, corticosteroids, benzodiazepines, muscle relaxants, low-dose antidepressants, and opioids [24]. Pharmacological management using NSAIDs (ibuprofen, piroxicam) has been shown in several controlled trials to be ineffective when compared with placebo [24,32,49]. However, one study using the NSAID naproxen shows a positive reduction in pain when compared with placebo [24,80]. In systematic reviews of the evidence for pharmacological treatments for TMD, there is a probable effect of the amitriptyline, clonazepam, and diazepam [49], but a more recent review from the Cochrane library suggests that there is insufficient evidence primarily based on the poor quality of the studies [60]. Evidence from RCTs shows effectiveness of cyclobenzaprine and gabapentin for TMD [41]. Thus, treatment with antidepressants, anticonvulsants, and muscle relaxants appears to reduce pain in people with TMD and orofacial pain.

For painful limited jaw opening, successful treatment with arthrocentesis (TMJ lavage, placement of medications into the joint) is reported in 70–90% of cases [25]. For internal derangement, surgery is utilized only after unsuccessful nonsurgical treatment, in people with significant pain and dysfunction, and if there is imaging evidence of pathology [25]. Surgical interventions include arthroscopy, condylotomoy, and disk repositioning or diskectomy [25].

For people with internal derangement, one common treatment is a splint to correct jaw alignment. However, there is inconclusive evidence for the use of splints or occlusional adjustment (modifying bite) for the treatment of TMD to reduce pain when compared with no treatment or placebo [2]. As with all TMD disorders conservative physical therapy treatment involving exercise to increase ROM and strength of the jaw muscles and modalities to reduce pain is recommended (see below). In advanced cases that are unresponsive to conservative treatment, surgery is often recommended and is effective [3,4,25].

Psychological Management/Self-Care

Self-care management is a common treatment for people with TMD. Self-care strategies include education, resting during pain, relaxation techniques, massage, hot and/or cold packs, and stretching and/or exercise (see Chapter 9). Positive effects for a self-care strategy to reduce pain and activity interference were confirmed in systematic reviews [14].

Brief cognitive-behavioral therapy for TMD is also efficacious in reducing

pain, improving coping skills, and lessening activity interference. Efficacy of therapy is increased when combining with self-care management, and some treatment effects are maintained for long term [1]. Future studies will need to determine the optimal number of treatments, and effects of cognitive-behavioral therapy with other treatments such as physical therapy.

Physical Therapy Management

Physical therapy treatment for TMD involves education on pain mechanisms, disease, posture, exercise, stretching, and soft tissue massage. Use of heat, cold, or TENS can help to reduce pain to allow the patient to exercise and stretch the soft tissue. It should be noted that though these therapies are recommended treatments for people with TMD, there are minimal RCTs, and thus systematic reviews, to support the effectiveness of these treatments (see Table 18-4).

Recommendations for stretching exercises and manual therapy are generally aimed at increasing ROM. Clinical trials show that home exercise stretching and manual therapy aimed at stretching soft tissue around the jaw muscles increase jaw opening and in some cases decrease pain [31,43,54,57]. Postural exercise training by physical therapists also significantly improves pain and pain-free ROM of the jaw [84]. Some studies, however, do not show an increased effect with stretching exercises, applied by a physical therapist or the patient in a home program when compared with self-management strategies [15,54]. Although the most common physical therapy treatments are aimed at increasing flexibility (stretching), strengthening, and endurance exercises, there are currently no studies examining the effects of strengthening or endurance exercises on pain associated with TMD [23,57]. Systematic reviews confirm the effectiveness of active and passive oral exercises that improve posture in reducing pain and improving ROM [51,52]. As other musculoskeletal pain conditions respond to a strengthening program, this may be an important component to the exercise program. Future studies should assess the effectiveness of different types of exercise programs in individuals with TMDs using an RCT design.

TABLE 18-4 **Evidence for Physical Therapy Treatments for Headache and TMD**

Disease	Treatment	Type of Study	Results
Migraine	Postural, cervical ROM, strengthening exercises	RCT	Effective only when used if unresponsive to relaxation and biofeedback
Migraine	Spinal manipulation of cervical spine	Cochrane Review	Reduces frequency, severity and disability, weak evidence
Migraine	Exercise	RCT	Significant decrease in headache frequency; similar to treatment with relaxation therapy and topiramate
Tension-type headache	Massage, relaxation, stretching, and home exercise	RCT and CT	Reduces frequency, analgesic consumption, and improves quality of life
Tension-type headache	Manual therapy	Meta-analysis	Manual therapy more effective than no treatment or pharmacological treatments; reduces headache frequency, intensity, and duration
Tension-type headache	Spinal manipulation	Systematic review	4/5 trials show improvements in headache; inconclusive
Tension-type headache	Trigger point focused massage	RCT	No more effective than placebo
Tension-type headache	Physical therapy (massage, relaxation, exercise)	RCT	Reduced headache frequency and analgesic consumption
Tension-type headache	Physical therapy (education, massage, exercise)	CT	Reduced headache frequency, improved quality of life; long-term effect at 1 year
TMD	Home exercise and manual therapy	RCTs	Reduces pain and improves jaw function
TMD	High-frequency TENS	RCT	Reduces pain and EMG activity
TMD	Oral exercises	Systematic review	Reduce pain and improve ROM
TMD	TENS	RCT	High-frequency TENS reduces pain and EMG activity; low-frequency TENS reduces EMG activity; TENS provides additional relief above pharmaceutical treatments
TMD	Low-level laser therapy	Systematic review	No different from placebo for pain; improvement in jaw ROM
TMD	Massage with occlusional splint	RCT	Reduced TMD pain when compared with treatments in isolation
TMD	Adding US, massage, or stretching by physical therapy to self-care program	RCT	No different from self-care

Abbreviations: ROM, range of motion; TMD, temporomandibular joint disorder; TENS, transcutaneous electrical nerve stimulation; RCT, randomized controlled trial; EMG, electromyograph; US, ultrasound.

Heat and cold packs used for control of pain are inexpensive and can be self-administered. However, there is no research to support or refute their effectiveness for TMD. High-frequency conventional TENS reduces pain and decreases EMG activity of the masticatory muscles in people with TMD [67], whereas low-frequency TENS reduces EMG activity [44]. A single treatment of either sensory stimulation or motor stimulation low-frequency TENS reduced EMG activity of the masticatory muscles similarly and improved interocclusal distance [56]. Additionally, two 30-minute TENS treatments in combination with

pharmaceutical treatment provided additional pain relief when compared with pharmaceutical treatment alone [73]. However, it should be noted that these studies were small with short-duration TENS treatments. A recent systematic review showed that low-level laser therapy (n = 14,454 subjects) was not better than placebo in reducing chronic TMD pain, but improved ROM of the jaw including jaw opening and protrusion [10]. Addition of ultrasound (US), massage, and stretching by a physiotherapist, or heat, massage, and stretching by the patient to a self-care program provided no additional effect on pain, pressure pain thresholds, or function; both treatments worked equally well [15,54]. However, in a group of patients instructed in using a home program of heat, massage, and stretching, there was an increase in jaw opening [54]. In a small RCT (n = 15/group), combining massage with an occlusional splint reduced signs and symptoms of TMD when compared with the treatments in isolation [35]. Thus, physical therapy should be aimed at improving function and posture with the use of education, exercises, and manual therapy. Modalities such as laser therapy, TENS, heat, and cold should be used as necessary to reduce pain. There is evidence from a limited number of RCTs to support the efficacy of TENS and laser therapy, as well as education, exercise, and manual therapy. Future clinical RCTs with adequate power will need to expand these studies by defining optimal treatment parameters, and examine effects of endurance and strengthening exercises.

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CHAPTER 19

Low Back Pain

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Spinal pain has an adverse societal impact because it is a common source of persistent pain and disability. This chapter reviews a specific type of spinal pain, low back pain (LBP), which will be operationally defined as pain originating between T12 and the gluteal fold [17]. LBP can also occur with leg pain, which has been operationally defined as painful symptoms distal to the gluteal fold or the knee. Clinically, the two primary patterns of leg pain are "referred," in which structures other than a lumbar nerve root are implicated as the source of symptoms, and "radicular," in which a specific lumbar nerve root is implicated. LBP that occurs following injury at work is often referred to as "work-related" or "occupational" LBP.

This chapter will review the clinical presentation and epidemiology of LBP and discuss examination techniques and common treatments. Individual studies, systematic reviews, and clinical practice guidelines from the peer-reviewed literature will be emphasized. This chapter is not intended to provide an exhaustive review of LBP; rather the overall goal is to provide appropriate context for effective, evidence-informed management of LBP.

GENERAL PRESENTATION OF LBP

Causes of LBP

Definitive causes of LBP are lacking in the literature. The development of LBP is believed to be multifactorial, potentially related to combinations of physical loading, physical characteristics, and genetic, biological, behavioral, psychological, anatomical, and societal factors [86]. It is beyond the scope of this chapter to review this entire literature, so only the example of lumbar anatomy and imaging studies will be used to demonstrate the difficulty in

determining definitive causes of LBP. Traditionally, abnormal lumbar anatomy (herniated disk, spinal stenosis, or exaggerated lumbar lordosis) was believed to be causative of LBP. However, subsequent imaging studies have indicated that abnormal lumbar anatomy is not always associated with LBP, and that LBP can occur when lumbar anatomy is normal. Specifically, Stadnik et al. [71] reported that 81% of asymptomatic patients have evidence of a bulging disk at some spinal level. Furthermore, Savage et al. [67] reported that 32% of asymptomatic subjects have abnormal lumbar anatomy, whereas only 47% of subjects who are experiencing LBP have abnormal lumbar anatomy, as identified on imaging studies. Abnormal lumbar anatomy is also not strongly linked with severity of symptoms in those experiencing LBP. Herno et al. [37] demonstrated a poor correlation between LBP symptoms and the degree of lumbar stenosis identified on magnetic resonance imaging (MRI). George et al. [29] reported no difference in severity of LBP or in functional limitations caused by LBP based on the amount of lumbar lordosis measured on radiograph.

The lack of a definitive relationship between LBP and lumbar anatomy is only one example of the difficulty of identifying specific causes of LBP. Similar problems exist for other risk factors. For example, there is a promising link between certain genetic factors and lumbar disk degeneration; however, a strong genetic link to the clinical presentation of LBP has not been identified [2]. Therefore, many different risk factors have the potential to cause LBP, without any single primary factor currently identified in the literature.

Definitive and specific anatomical diagnostic criteria for LBP are currently not offered in the peer-reviewed literature, and, as demonstrated, there are a number of potential but uncertain causes. The American College of Physicians/American Pain Society (ACP/APS) recognizes three major but general types of LBP: (1) LBP associated with radiculopathy or spinal stenosis; (2) back pain associated with another specific spinal cause; and (3) nonspecific LBP [9]. The term *nonspecific* has been applied to pain in the low back that is not related to underlying pathology (i.e., related to tumor, infection, or fracture) [17,31]. It has been estimated that up to 90% of LBP is nonspecific, and it is these nonspecific syndromes that have a substantial adverse impact on society [17,31]. Therefore, this chapter will focus on issues related to nonspecific LBP syndromes and will not include information related to conditions associated with specific spinal pathology (e.g., spinal stenosis or spondylolisthesis).

Epidemiology and Course of LBP

The prevalence of LBP is well documented in the literature, although estimates

vary widely owing to methodological differences. According to the 2011 Institute of Medicine (IOM) report, there were approximately 116 million adults in the United States suffering from chronic pain conditions. Data from the National Center for Health Statistics (NCHS) in 2009 indicated that the highest cause of chronic pain among age-adjusted rates of adults reporting pain was LBP at 28.1% [7,43]. Additionally, a population-based study from the Netherlands reported that LBP was the most common form of musculoskeletal pain reported by adults 25 years of age and older, with a point prevalence of 26.9% (95% CI = 25.5–28.3) [64]. One systematic review pooled higher-quality studies and provided point prevalence estimates ranging from 12% to 33%, 1-year prevalence estimates ranging from 22% to 65%, and lifetime prevalence estimates ranging from 11% to 84% [87]. In addition, the Department of Veterans Affairs Health System saw an increase in LBP prevalence by approximately 5% annually [69]. A study in North Carolina found that the prevalence of chronic LBP across all subgroups had more than doubled from 1992 through 2006.

In this same study in North Carolina, the rate of women across all ages with LBP more than doubled and the rate for men aged 45–54 more than tripled [23]. In the aforementioned Netherlands study, the point prevalence of LBP was 28.1% for women (95% CI = 26.1–30.1) and 25.6% for men (95% CI = 23.5–27.7) [64]. The IOM report also indicates that women report higher prevalence of LBP (30.1%) than do men (26%), on the basis of 2009 data from NCHS for age-adjusted rates of adults reporting pain in the previous 3 months [7,43]. Older age is also associated with higher prevalence of LBP [49,76], but the prevalence of LBP eventually levels off and declines in later decades of life [64]. The wide range of these prevalence estimates can be attributed to several factors, most notably the lack of a standard definition of chronic LBP.

The course of LBP is often viewed as one with discrete acute and chronic stages, with complete symptom resolution as a common occurrence. However, prospective studies indicate that recurrence is often experienced [85]. For example, 65% of patients with acute LBP who are followed for 1 year reported one or more additional episodes [5]. Von Korff has suggested operational definitions to help clinicians and researchers to better describe the course of LBP (Table 19-1) [84]. Although these definitions have not been universally adopted, they are a reflection of the actual course of LBP and may provide better clinical context, rather than simply indicating acute and chronic phases of the disease.

Prognostic factors for persistent LBP have also been investigated in the literature, and several factors are consistently associated with poor outcome. The co-occurrence of leg pain with LBP, high initial pain, high disability, and

psychological distress are indicators of poor outcome [1,11,51,65,70,78]. In addition, although obesity has not been linked to causing LBP, it is associated with poor outcomes following onset of LBP [50]. Specific to studies of work-related LBP, severe leg pain, high disability, poor general health, and unavailability of light duties are all associated with still receiving compensation 3 months after an injury [22,58]. A systematic review of factors found that longer sick leave in patients with acute low back pain is associated with higher disability levels, older age, female sex, more social dysfunction or isolation, heavier work, and receiving higher compensation [73].

Societal Impact of LBP

The most recent estimates indicate that in 2010 chronic pain conditions cost the United States between $500 and $635 billion overall, with health care costs specifically contributing to between $261 and $300 billion in expenditures [28]. The Center for Disease Control estimated that disability from all causes costs approximately $300 billion annually, with back/spine problems and arthritis being the two leading causes [6]. As LBP has been identified as one of the leading causes of chronic pain and is strongly associated with disability, it accounts for a considerable amount of the overall annual cost of chronic pain, both in lost work productivity and health care expenditures. One study found that back pain itself contributes to expenditures greater than $100 billion each year, with two-thirds of this related to lost wages and decreased productivity [46]. Another study found that LBP was responsible for almost 3% of the increase in U.S. health care expenditures from 1987 to 2000 [79]. Estimates from an additional study show that medical costs (adjusted for inflation) for individuals with spine problems increased by 65% from 1995 to 2007; these estimates showed much higher expenditures in individuals with spine problems compared with individuals without spine problems in both 1995 and 2007 [57].

TABLE 19-1 **Operational Definitions for Describing the Course of LBP**

Descriptor	Operational Definition of an Episode of LBP
Transient back pain	Present for no more than 90 consecutive days and does not recur over a 12-mo period
Recurrent back pain	Present for less than half the days in a 12-mo period and occurs in multiple episodes over the year
Chronic back pain	Present for at least half the days in a 12-mo period in single or multiple episodes
Acute back pain	Onset is recent and sudden and does not meet the previously defined criteria for recurrent or chronic pain
First onset	First occurrence in the patient's lifetime
Flare-up	Distinct phase (with definable beginning and end points) of pain superimposed on a chronic or recurrent course; refers to a period when the pain is markedly more severe than is usual for the patient

Abbreviation: LBP, low back pain.

Persistent LBP also significantly limits individuals' capacity to work and is associated with the inability to obtain or maintain employment [72] and with reduced productivity at work [75]. Data from the NCHS showed that the most common cause of disability was joint pain, followed by LBP; individuals with LBP accounted for 51.6% of adults with chronic pain in the past 3 months who also reported difficulty with basic activities and 55% of adults who reported limitations with complex activities [7,43]. In Australia, 53% of adults reported some disability from LBP during a 6-month period [88]. These estimates of individual impact and the previously reviewed societal costs highlight the concurrent growing concern for increased LBP prevalence. Furthermore, owing to its increased and growing prevalence, it is not surprising that LBP is a common reason to seek health care from physical therapists [16], accounting for approximately 25% of all patients discharged from outpatient clinics [44]. Effective management of LBP is a high priority for physical therapists so that the societal burden of these pain syndromes is lessened.

PHYSICAL THERAPY MANAGEMENT

Many different clinical practice guidelines have been published on the management of LBP by physical therapists, and it is beyond the purpose of this chapter to review each of them. Instead this chapter will use the LBP clinical practice guidelines from the 2012 Orthopedic Section of the American Physical Therapy Association (APTA) [14] as the primary reference for optimal physical therapy management. These guidelines were developed after a systematic literature search, extensive and careful consideration of published evidence, and

external peer review. Once completed, the Orthopedic Section Clinical Practice Guidelines for Low Back Pain were sent to the National Guideline Clearing house (Agency for Healthcare Research and Quality; www.guideline.gov) for final approval and access as a public resource. The Orthopedic Section Guidelines provided recommendations for examination, intervention, and monitoring for patients with LBP. This chapter will also discusses psychologically informed practice, a practice approach used in combination with guideline recommendations for individuals with musculoskeletal pain demonstrating high risk for poor outcomes owing to increased levels of psychological distress.

Physical Therapy Examination

Red Flag Screening

Examination of LBP should start with consideration of red flags. The goal of this part of the examination is to determine if physical therapy treatment of LBP is appropriate or if referral to other providers may be indicated. Red flags are signs and symptoms that LBP may be related to serious medical pathology such as a tumor, fracture, or infection. Positive red flags are an indication that additional information is warranted before treatment can begin and leads to a decision on whether patients should be referred for additional diagnostic testing. Red flag identification typically starts with a medical questionnaire followed by a medical history to confirm positive answers [4]. Common red flags for LBP include constant pain, unexplained weight loss, concurrent fever, a history of cancer, and change in bowel and bladder function. Red flag identification has not been thoroughly investigated in clinical studies, but available studies indicate that accuracy may be lacking for identification of underlying spinal pathology. For example, a primary care inception cohort study of acute LBP in Australia recorded 11/1172 (0.9%) patients with serious pathology and of those 11 patients, only 5 were identified at initial consultation [36]. Also, in a systematic review investigating the accuracy of red flags for identifying spinal fracture or malignancy only a small subset of the 53 red flags considered improved diagnostic accuracy [18]. Providers should understand how these issues impact clinical decision making and be aware of updated research that may provide better options for identifying underlying pathology.

Yellow Flag Screening

After red flags are considered, the examination should then proceed to screening for yellow flags. The identification of psychological factors indicative of poor prognosis has been advocated most consistently for yellow flag screening in LBP [35,52]. The specific psychological factors used in yellow flag screening vary, but commonly include assessment of depression, fear-avoidance beliefs, and pain catastrophizing [26,33,77] (see Chapter 6). These factors have been shown to be key indicators for risk of chronicity and poor outcomes in patients with LBP [10,40,60].

One way yellow flag screening can be completed is through the use of multidimensional questionnaire, for example, the STarT Back Screening Tool (SBT) (see Chapter 6). The SBT is a self-report questionnaire that has been shown to be an efficient way to identify psychological barriers to LBP recovery in primary care and physical therapy settings [39]. It provides an initial risk assessment, categorizing individuals into one of three stratified groups—low risk, medium risk, and high risk. Importantly, changes over time in pain and disability outcomes have been shown to be related to SBT risk categorization [25]. This suggests overall SBT scores may provide useful prognostic information for physical therapists and may also be particularly important in clinical decision making for treatment and monitoring progress [3,25].

Specifically, risk assessment can be used to determine the intensity of physical therapy. Low-risk individuals typically require minimal skilled physical therapy services, whereas medium-risk and high-risk individuals are appropriate candidates for further skilled treatment. Individuals identified as high risk will require more focused psychological assessment using full questionnaires for the constructs of interest. Appropriate measures for specific psychological constructs are two questions from the Primary Care Evaluation of Mental Disorders patient questionnaire to assess for depression symptoms, the Fear-Avoidance Beliefs Questionnaire to assess for fear-avoidance beliefs in response to pain, and the Pain Catastrophizing Scale to determine the level of catastrophizing during pain episodes. When warranted, regular administration of these full assessments ensures sensitivity to change is captured more accurately for each of these psychological factors. In addition, for therapists interested in graded exposure approaches, patient responses particularly on the Fear of Daily Activities Questionnaire (FDAQ) may identify functional activities that should be targeted during treatment [30].

Physical Examination

The physical examination should include techniques that determine one of three

phases of LBP—acute, subacute, and chronic—and the presence or absence of additional symptoms—related or referred lower extremity pain, radiating pain, and movement and coordination deficits. Determination of phase and symptoms will assist the physical therapist in properly categorizing patients into the Orthopedic Section Guideline–endorsed subgroups; this is an important step in the examination process as subgroups determine suggested evidence-based treatment options. Suggested physical impairment techniques and measurements used to establish subgroup categorization are described in Table 19-2.

On the basis of screening for cognitive factors and this impairment battery of tests, individuals with LBP can be classified according to the International Classification of Functioning, Disability and Health (ICF)–based subgroups found in the Orthopedic Section Guidelines: (1) Acute LBP with Mobility Deficit; (2) Subacute LBP with Mobility Deficits; (3) Acute LBP with Movement Coordination Impairments; (4) Subacute LBP with Movement Coordination Impairments; (5) Chronic LBP with Movement Coordination Impairments; (6) Acute LBP with Related (Referred) Lower Extremity Pain; (7) Acute LBP in Radiating Pain; (8) Subacute LBP with Radiating Pain; (9) Chronic LBP with Radiating Pain; (10) Acute or Subacute LBP with Related Cognitive or Affective Tendencies; and (11) Chronic LBP with Related Generalized Pain. These subgroups were established on the basis of moderate evidence and as previously mentioned correspond to suggested treatment options that will be discussed later in further detail (see Table 19-3).

TABLE 19-2 **LBP Impairment Assessments**

Suggested Impairment Assessments	Description
Lumbar active range of motion	Measure active lumbar flexion, extension, and side-bending
Segmental mobility	In prone position assess lower thoracic and lumbar spine segmental movement
Pain provocation with segmental mobility	Assess for pain region and pain response during segmental mobility testing described above
Centralization during movement	Assess for presence of centralization (symptom location moves proximal) during application of active and passive movement
Prone instability test	(1) With individual in prone trunk position and feet off table resting on floor, assess for pain response during application of posterior-anterior pressure to lumbar spine (2) Repeat assessment with individual's legs lifted off floor (+) Pain in position (1); substantial reduced pain in position (2) (−) Pain in position (1) that does not substantially reduce in position (2)
Assessment for aberrant movement	Assess for presence of the following: (a) painful arc during lumbar flexion or return from flexion (b) instability catch (c) Gower sign (d) reversal of lumbopelvic rhythm
Straight leg raise	Assess for presence or absence of lower extremity radiating/radicular pain during supine straight leg raise
Slump test	With individual seated assess for symptoms during sequential addition of cervical flexion, knee extension, then ankle dorsiflexion (+) Reproduction of symptoms in final position and relief when cervical spine is subsequently extended and/or knee is flexed, and/or ankle is plantarflexed (−) Reproduction of symptoms not achieved
Trunk muscle power and endurance	Assess power/endurance in trunk flexors, trunk extensors, lateral abdominals, transversus abdominis, hip abductors, and hip extensors
Passive hip range of motion	Measure passive hip rotation, flexion, and extension

Abbreviation: LBP, low back pain.

Source: Adapted from *Orthopaedic Section Clinical Practice Guidelines for Low Back Pain*.

Outcome Measures

Finally, physical therapists should administer appropriate validated outcome measures during the initial evaluation to capture baseline status and to monitor clinical change during the course of treatment. The Ostwestry Disability Index and Roland-Morris Disability Questionnaire are region-specific instruments that can be used to establish patient-reported disability. The Numeric Pain Rating Scale and Visual Analog Scale can both be used for the specific assessment and monitoring of patient-reported pain, whereas the Medical Outcomes Survey–Short Form 36 should be used to capture other domains related to LBP including function, work disability, health status, and patient satisfaction. Evidence supporting the use of additional performance-based, clinician-measured outcomes is limited. The previously listed patient-reported outcomes appear

more important for standardized baseline assessment and continued monitoring. However, performance-based outcomes, such as the Functional Capacity Evaluations, do provide a method for assessing and monitoring activity and participation restrictions.

TABLE 19-3 LBP Subgroups and Corresponding Treatment Options

LBP Subgroup	Suggested Treatment Options
Acute LBP with Mobility Deficit	Manual therapy, therapeutic exercise for mobility, patient education on maintaining activity
Subacute LBP with Mobility Deficits	Manual therapy, therapeutic exercise for mobility, patient education on maintaining activity
Acute LBP with Movement Coordination Impairments	Neuro-muscular reeducation for stability, patient education on self-care
Subacute LBP with Movement Coordination Impairments	Neuromuscular reeducation for stability, manual therapy, therapeutic exercise for strength, patient education for self-care and community and work reintegration
Chronic LBP with Movement Coordination Impairments	Neuromuscular reeducation for stability, manual therapy, therapeutic exercise for strengthening, patient education for community and work reintegration
Acute LBP with Related (Referred) Lower Extremity Pain	Therapeutic exercise for mobility, manual therapy, and potentially traction; patient education for positioning to promote centralization of symptoms
Acute LBP in Radiating Pain	Patient education for positioning to reduce compression, potentially traction, manual therapy, nerve mobility exercises
Subacute LBP with Radiating Pain	Manual therapy, potentially traction, nerve mobility exercises
Chronic LBP with Radiating Pain	Manual therapy, patient education for pain management strategies
Acute or Subacute LBP with Related Cognitive or Affective Tendencies	Use of psychologically informed practice principles
Chronic LBP with Related Generalized Pain	Use of psychologically informed practice principles (if indicated), low intensity, prolonged therapeutic exercises

Abbreviation: LBP, low back pain.

Source: Adapted from *Orthopaedic Section Clinical Practice Guidelines for Low Back Pain*.

Physical Therapy Interventions

After the above components of an initial examination are completed, specific interventions are considered for inclusion in the treatment plan. Numerous systematic reviews [1,20,24,27,32,34,38,47,61,63] have investigated the efficacy of treatments for LBP. The Orthopedic Section Guidelines indicate five specific treatment options with moderate to strong supporting evidence. These are (1) manual therapy (strong evidence); (2) trunk coordination and strengthening and endurance exercises (strong evidence); (3) centralization and directional preference exercises (strong evidence); (4) patient education and counseling (moderate evidence); and (5) progressive endurance exercise and fitness activities (strong evidence). Traction is also mentioned, but with indication of

conflicting evidence; preliminary evidence supports use in patients with peripheral symptoms or a positive crossed straight leg raise, but opposing moderate evidence discourages use for patient with acute or subacute, nonradicular LBP or chronic LBP. Additionally, a Cochrane review that included 32 trials concluded that traction was not effective for acute, subacute, or chronic LBP [89]. Flexion exercises and lower quarter nerve mobilization procedures are also included but found to have weak evidence.

Developing a Treatment Plan for Medium- and High-Risk Patients

Subgroups and initial risk assessment identified during examination should be used to develop an appropriate, individualized treatment plan (see Fig. 19-1). The Orthopedic Section Guidelines recommend that optimal use of the above treatment options is dependent on the ICF subgroup classification. Table 19-3 lists each subgroup and indicates the suggested evidence-based treatment options. Individual risk assessment should also be considered. Low-risk individuals (likely to include some of the acute subgroups) typically require minimal to no further physical therapy services on the basis of severity of symptoms during the physical examination. Medium-risk individuals (likely to include most of the subacute and some of the acute subgrouped individuals) are typically appropriate for physical therapy, and treatment should follow suggestions from the Orthopedic Section Guidelines as described in Table 19-3. High-risk individuals will likely include, but not be limited to, those individuals also classified by subgrouping as having Acute or Subacute LBP with Related Cognitive or Affective Tendencies or as having Chronic LBP with Related Generalized Pain. To optimize recovery in this high-risk group, treatment should include options recommended by the Orthopedic Section Guidelines as well as cognitive behavioral strategies to reduce psychosocial barriers [48,54,55].

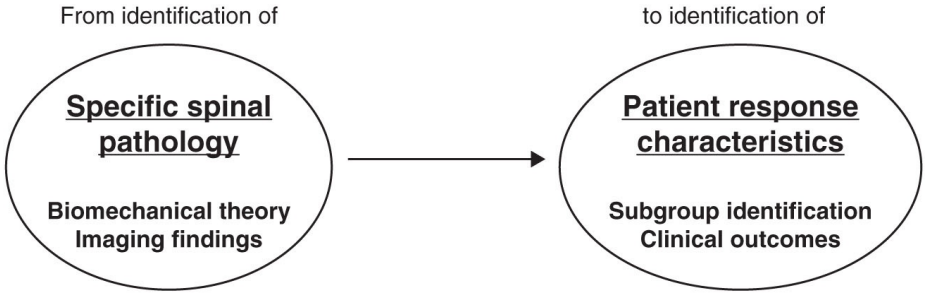

FIGURE 19-1 Paradigm shift in physical therapy treatment philosophy.

Psychologically Informed Practice

Treatment for high-risk individuals described above is termed *psychologically informed practice*. The addition of cognitive behavioral strategies (see Chapter 16) can potentially modify these factors and improve patient prognosis; it is therefore an important practice approach for physical therapists to consistently utilize them [54]. Studies performed in primary care settings referring individuals for physical therapy services support the use of cognitive behavioral treatment for LBP. A randomized controlled trial (RCT) found that the addition of cognitive behavioral treatment strategies was superior (improved patient outcomes and increased cost-effectiveness) to standard treatment alone in a group of primary care LBP patients [48]. Use of SBT and stratified care on the basis of risk assessment has also been shown to be effective. An RCT and a prospective cohort study both found that the use of stratified care led to improved disability and reduced time off work [21,41]. The prospective comparison additionally found stratified care to be more cost-effective [21]. For physical therapists, psychologically informed practice offers a comprehensive, patient-centered approach that can be integrated into routine practice and combined with Orthopedic Section Guideline recommendations as necessary. It is, however, important to note that implementation of cognitive behavioral treatment strategies may require additional training beyond general physical therapy education in order to be most effective [55]. In addition, routine monitoring with the aforementioned psychological measures is important to ensure psychological distress is being reduced, as referral to psychological services may otherwise be warranted.

MEDICAL MANAGEMENT

LBP is a common reason for people to seek health care, not only from physical therapists, but also from physicians and alternative and complimentary practitioners [13,15,19,56,68,80,83,91]. Only 25–50% of individuals who experience LBP seek treatment [13,42], and these patients have higher disability and pain intensity in comparison with those who do not seek health care [13,42,59]. Because of the common use of other medical services, physical therapists must be aware of general trends in medical management of LBP. The importance of recognizing subgroups of LBP, self-care options, psychosocial barriers, and the consideration of a wide range of potential treatments for those

who do not improve as expected has recently been stressed in the medical management of LBP.

Guidelines for Medical Diagnosis and Treatment of LBP

The ACP/APS Clinical Guidelines serve as the primary source of medical recommendations for this chapter [9]. The guideline recommendations for diagnosis of LBP include the performance of a focused examination with the primary purpose of determining the type of LBP [9]. As mentioned previously, these major types of LBP include (1) LBP associated with radiculopathy or spinal stenosis, (2) back pain associated with another specific spinal cause, and (3) nonspecific LBP [9]. Assessment of psychological risk factors is recommended for all individuals to serve the purpose of identifying those at risk for developing persistent LBP. One study has investigated the use of the SBT in primary care settings to assist physicians in referral of LBP individuals to physical therapist [39]. The SBT was found to be an effective screening and referral tool, suggesting it could be utilized to improve consistency and appropriateness of referrals [39].

Routine imaging or other diagnostic testing is not recommended for patients with nonspecific LBP. Diagnostic imaging is recommended for patients who have severe or progressive neurological deficits or when serious underlying conditions (red flags) are suspected from the history. MRI is the recommended diagnostic imaging technique for patients with lumbar spinal stenosis or suspected radiculopathy. Computed tomography (CT) is recommended for diagnostic imaging for candidates for surgery or epidural steroid injection. However, routine imaging for nonspecific LBP has been shown to be harmful, as it can result in unnecessary medical costs [8], follow-up testing, referrals, and recommendations for invasive procedures of limited effectiveness [8,53,82].

The ACP/APS Clinical Guidelines recommend treatment of LBP to include educational options of providing factual information on the course of LBP, encouraging patients to return to normal activities, and providing information about self-care options [9]. Medication should start with acetaminophen or nonsteroidal anti-inflammatory drugs (NSAIDs) for those with acute LBP, although the use of skeletal muscle relaxants, benzodiazepines, and opioids are also acceptable for acute LBP. Medication for chronic LBP can include acetaminophen, NSAIDs, antidepressants, benzodiazepines, and opioids (more details on pharmacological management of acute and chronic pain can be found in Chapter 15). A double-blinded, RCT determined that the efficacy of acetaminophen (paracetamol) for the treatment of acute LBP was no better than

placebo for recovery of episodes [90]. This trial was one of the first tests of NSAID recommendations for guidelines, and this new evidence may result in changes to subsequent LBP treatment guidelines. The ACP/APS Clinical Guidelines also typically suggest nonpharmacological treatment options only for those patients whose symptoms do not improve. Many of these nonpharmacological options were included in the ACP/APS Clinical Guidelines and are reported in Table 19-4.

A current nonpharmacological treatment option that is of interest to physical therapists is trigger point injections and use of dry needling to reduce trigger points within the muscle. Trigger points are theorized to be taut bands of tissue that result in muscle pain. A review of best evidence regarding the existence of trigger points, identification of trigger point locations, and their direct causation of pain, however, shows little to no support for this theory [66]. A recent randomized clinical trial did show support for the use of trigger point dry needling on the lower trapezius muscle in individuals with mechanical neck pain; results showed that dry needling at identified active trigger points resulted in more significant decreases in pain intensity, pressure pain threshold, and disability compared with dry needling at other locations in the lower trapezius muscle [62]. Another recent RCT investigating effectiveness of trigger point dry needling for the treatment of plantar heel pain did show positive support for the intervention, finding significant decreases in plantar heel pain in a dry needling group compared with a sham needling group [12]. However, there was also a significant increase in minor, transitory adverse events (e.g., needle stick pain) and some delayed adverse events (e.g., bruising) from dry needling [12]. Owing to questions of biological plausibility, limited clinical evidence, potential for adverse events, and limited generalizability across conditions, support for this theory remains speculative. Furthermore, the effects of dry needling are short term, with recent evidence showing treatment effects may not differ from well-designed placebos; thus it should be used in conjunction with an exercise program [74]. Caution should be taken in considering the inclusion of this treatment in the management of LBP.

TABLE 19-4 **Current Treatment Recommendations for Acute and Chronic LBP**

Acute LBP	Chronic LBP
Self-Care Methods	
Advice to remain active	Advice to remain active
Books, handouts	Books, handouts
Superficial heat	
Pharmacological Therapies	
Acetaminophen	Acetaminophen
NSAIDs	NSAIDs
Skeletal muscle relaxants	Antidepressants
Benzodiazepines	Benzodiazepines
Tramadol, opioids	Tramadol, opioids
Nonpharmacological Therapies	
Spinal manipulation	Spinal manipulation
	Exercise therapy
	Massage
	Yoga
	Cognitive-behavioral therapy
	Progressive relaxation
	Intensive interdisciplinary rehabilitation

Abbreviations: LBP, low back pain; NSAIDs, nonsteroidal anti-inflammatory drugs.

Source: Adapted from Chou and Shekelle [10].

INTERDISCIPLINARY MANAGEMENT OF CHRONIC LBP

Chronic LBP has a multifactorial etiology, so optimal management may be best provided by an interdisciplinary team promoting an active approach to pain management. Many potential members of this team exist, but most teams consist of a core unit including a physician, psychologist, and physical therapist. For more details on interdisciplinary pain management, see Chapter 14. In this setting, the physician is responsible for overall medical management, including pharmacological therapies. Psychological management includes treatments that use cognitive strategies, either alone or in combination with behavioral - approaches supported by evidence for treatment of chronic LBP [9]. Physical therapy management includes improvement in physical impairments and tolerance of functional activities. Physical therapy treatment may also require the implementation of cognitive-behavioral strategies as demonstrated by the use of psychologically informed practice; this would be best implemented through co-management with psychologists' or psychiatrists' input, in addition to advanced

training in these interventions [54]. Another interdisciplinary care option is an interdisciplinary pain rehabilitation program; this intensive approach sometimes keeps patients in treatment for up to 8 h/d. Compelling information that such approaches provide cost-effective alternatives for the treatment of chronic pain exists [9,81], although this evidence is not absolute [45,61].

SUMMARY

In summary, LBP is a musculoskeletal pain condition that is high in prevalence, with multiple potential causes, and costly to society. LBP can often be effectively managed through a combination of medical, psychological, and physical therapy treatment interventions that integrate psychologically informed practice. Effective physical therapy management of LBP includes identification of both physical and psychological impairments in order to develop individualized treatment plans and optimize recovery.

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CHAPTER 20

Neck Pain

Michele Sterling

Neck pain is operationally defined as pain extending from above the spines of the scapula to the superior nuchal line, with or without radiation to the head, arms, or trunk [19]. Radiation of pain to the upper limbs or head may be pain referred from somatic structures in the neck or implicate the involvement of peripheral nerve tissue ranging from irritation to nerve root compression, the latter being termed cervical radiculopathy [30].

Neck pain can occur as a consequence of systemic diseases such as inflammatory arthritis or tumors but by far the most common causes are benign where the origin of the pain is related to somatic structures of the cervical spine. The precise anatomical structure, if there is one, cannot usually be determined and thus the neck pain is defined as nonspecific. Neck pain can occur as a result of a traumatic injury, for example, a motor vehicle crash, fall, or sports incident, and in these cases it is defined as whiplash-associated disorders (WAD). It can also be nontraumatic in nature with no specific event or injury being attributed to its onset. It has been argued that this differentiation should not be made and that neck pain be considered and classified as one condition [19] but some evidence suggests differences in the underlying biological and psychological processes between neck pain of traumatic and nontraumatic origins [6,12,50] and these will be further discussed later in this chapter.

EPIDEMIOLOGY, SOCIETAL IMPACT, AND DIAGNOSIS

Neck pain occurs commonly throughout the world. The recent Global Burden of Disease study found that the global age-standardized point prevalence of neck pain was estimated to be 4.9% (95% confidence intervals [CI] = 4.6–5.3) [25]. It was higher in women (mean: 5.8%; 95% CI = 5.3–6.4) than in men (mean:

4.0%; 95% CI = 3.7–4.4) and the age and sex distribution across world regions was similar [25]. Neck pain was ranked fourth out of 291 conditions contributing to global disability [25], with low back pain, major depressive disorder, and iron-deficient anemia ranked first to third [71]. In terms of overall burden (measured with DALYS: disability adjusted life years), neck pain was ranked 21st [71].

The Bone and Joint Decade 2000–2010 Task Force review on neck pain found that 50–80% of people in the general population who report neck pain at some point will also report neck pain 1–5 years later, but it could not be determined if this pain was persistent (ongoing) or recurrent (comes and goes) over these time periods [3]. With respect to WAD, there is evidence available indicating that following the injury, 50% of those injured will develop persistent pain and disability to some extent and that the trajectory is one of some initial improvements in the first few months with the persisting rather than recurrent symptoms [56].

Prognostic or risk factors for neck pain can be viewed as either being risk factors for the new onset of neck pain or factors that predict chronic neck pain after its initial onset. In a best evidence synthesis, Hogg-Johnson et al. [23] identified nonmodifiable risk factors for the onset of neck pain as older age, female gender, and genetic factors, and modifiable risk factors as smoking, exposure to tobacco smoke, and poorer psychological health but the strength of the evidence is limited by a lack of prospective cohort studies. As with most other nonspecific musculoskeletal pain conditions, identification of cervical anatomical pathologies, such as degenerative changes, has not been shown to be risk factors for neck pain [23].

In people already with neck pain, younger people have a better prognosis with additional modest predictive effects of poor health and prior pain and at least moderate effects for some psychological factors including poor psychological health, and worrying, becoming angry, or frustrated in regard to the neck pain [3]. Several systematic reviews of prognosis following whiplash injury have been undertaken. The most consistent prognostic indicators for poor functional recovery include initially higher levels of pain and disability [5,73,75] with a recent meta-analysis indicating that initial pain scores of greater than 5.5 on a visual analog scale from 0 to 10 and scores of greater than 29% on the Neck Disability Index are useful cutoff scores for clinical use [74]. Other prognostic factors for poor recovery following whiplash injury have been identified, including psychological factors of initial moderate posttraumatic stress symptoms, pain catastrophizing, and symptoms of depressed mood [5,58,75]. Additionally, lower expectations of recovery have been shown to predict poor recovery [4,24]. In other words, patients who do not expect to recover well may

indeed not recover. Cold hyperalgesia has been shown to predict disability and mental health outcomes at 12 months postinjury [15,57,59]. Many patients with neck pain will be involved in some form of compensation process, whether related to worker's compensation or third-party road traffic crash compensation. There is evidence that compensation-related factors are associated with poorer health outcomes but the reasons for this are not clear [40].

The diagnosis of neck pain is usually made by self-reported symptoms, as in the vast majority of cases specific tissue damage or a peripheral lesion cannot be identified [10]. The exception to this is cervical radiculopathy where a combination of physical examination, electrophysiological testing, and imaging is capable of detecting neurological compromise in order to diagnose this condition [42,72]. Various classification systems for neck pain have been proposed. The Quebec Task Force (QTF) classification of whiplash injuries was put forward in 1995 [52] and it remains the classification method still currently used throughout the world for WAD. Although the QTF system is rather simplistic and based only on signs and symptoms, it allows practitioners and other stakeholders involved in the management of patients with WAD to have a common language about the condition. Most patients fall into the WAD Grade II classification (i.e., neck pain with some physical signs such as range of movement loss but no neurological deficit), although health outcomes for this group can be diverse and this has been outlined as one problem with the QTF system [53]. More recently, the Bone and Joint Decade Task force proposed a similar classification system that includes all neck pain, not only WAD [20] (Table 20-1). This system is yet to be validated and as such its clinical utility is not yet clear.

TABLE 20-1 **Proposed Classification System for Neck Pain [20]**

Stage	Operational Definition
Grade I neck pain	No signs or symptoms suggestive of major structural pathology and no or minor interference with activities of daily living; will likely respond to minimal intervention such as reassurance and pain control; does not require intensive investigations or ongoing treatment
Grade II neck pain	No signs or symptoms suggestive of major structural pathology, but major interference with activities of daily living; requires pain relief and early activation/intervention aimed at preventing long-term disability
Grade III neck pain	No signs or symptoms suggestive of major structural pathology, but presence of neurologic signs such as decreased deep tendon reflexes, weakness, and/or sensory deficits; might require investigation and, occasionally, more invasive treatments
Grade IV neck pain	Signs or symptoms of major structural pathology such as fracture, myelopathy, neoplasm, or systemic disease; requires prompt investigation and treatment

Note: The classification system included both traumatic (WAD [whiplash-associated disorders]) and nontraumatic neck pain. It has not yet been validated and it has been argued that WAD and nontraumatic neck pain should not be included in one system because of identified differences in nociceptive processing [50].

PATHOBIOLOGY OF NECK PAIN

As outlined earlier, a precise pathoanatomical diagnosis cannot usually be made in the majority of patients with nonspecific neck pain. In view of this, much research in recent times has focused on improving the understanding of the physiological and psychological processes that underlie neck pain conditions with the rationale that targeting these factors with specific interventions may improve outcomes.

There is overwhelming evidence showing that movement, muscle, and motor control changes in the neck and shoulder girdles are present in patients with neck pain. Study findings include inferior performance on tests of motor control involving the cervical flexor, extensor, and scapular muscle groups when compared with asymptomatic control participants; changes in muscle morphology of the cervical flexor and extensor muscles; loss of strength and endurance of cervical and scapular muscle groups; and sensorimotor changes manifested by increased joint repositioning errors, poor kinesthetic awareness, altered eye movement control, and loss of balance [12,13,29,69]. Although the majority of these movement/motor changes are seen in all neck pain regardless of onset, greater dysfunction appears to be more apparent in WAD (traumatic onset neck pain). For example, the presence of fatty infiltrate in the cervical flexors and extensors, clearly present in WAD but not in nontraumatic onset neck pain [12,14]. The cause of the fatty infiltrate and its implications for treatment is not clear.

Additionally, it seems that the sensory presentation of traumatic and nontraumatic neck pain is different with the inference being that nociceptive processing is different between the two forms of neck pain. Two recent systematic reviews have concluded that there is moderate evidence that the sensory presentation of widespread sensory hypersensitivity at sites both local and remote to the injured area found in chronic WAD indicates the presence of augmented nociceptive processing or sensitization within the central nervous system [62,70]. Later findings would support this with clear evidence of spinal cord hyperexcitability [33] as well as impaired descending inhibitory mechanisms [40]. Although there are some reports of similar findings indicative of central sensitization in nontraumatic neck pain when compared with healthy controls [28], direct comparisons of nontraumatic neck pain and WAD have shown more pronounced sensory disturbances in the latter traumatic neck pain group [6,12,50]. These findings suggest that different nociceptive processing mechanisms may underlie neck pain depending on whether or not it is of

traumatic onset and this could be one reason for apparently better responses to physical treatments in patients with nontraumatic neck pain [31,36]. It also suggests that neck pain classification systems will need to take these findings into account and that a single classification system for all neck pain may not be optimal. These proposals require further investigation.

ASSESSMENT CONSIDERATIONS FOR NECK PAIN

Although the majority of neck pain is benign, it is important to screen for red flags both to determine if physical therapy is indicated and to make necessary referrals for evaluation of more serious medical conditions such as tumor, fracture, infection, or inflammatory arthritis. Red flag signs for neck pain include constant pain, severe headache, unexplained weight loss, concurrent fever, history of cancer, history or rheumatoid arthritis, paresthesia, and anesthesia in the limbs and upper motor neuron signs [67]. In cases where there is a history of trauma, clinical guidelines recommend the use of the Canadian C-Spine Rule to determine the need for radiological investigation [38]. The Canadian C-Spine Rule uses a clinical decision algorithm that has high sensitivity and specificity to detect injuries such as fracture or dislocation [37].

As initial pain and disability levels are the most consistent prognostic indictors for poor recovery [3,5], it is mandatory that these factors are measured as the first step of physical clinical assessment. Guideline-recommended pain measures include the 11-point VAS scale or numeric rating scale and the recommended measure of disability is the Neck Disability Index due its clinimetric properties [7,38]. However, other measures are also acceptable and some include the Whiplash Disability Questionnaire and the Patient Specific Functional Scale [38].

Assessment of nociceptive processing should also be undertaken, particularly in patients with WAD as this may direct treatment to target such processes. Clinically, central sensitization may be suspected from subjective reports of the patient including reports of allodynia, high irritability of pain, cold sensitivity, and poor sleep due to pain, among others [55]. Physical tests may include the use of pressure algometers, and pain with the application of ice [35] or with demonstrated increased bilateral responses to the brachial plexus provocation test [54]. Questionnaires that evaluate neuropathic pain–like symptoms could also be used but they are yet to be fully evaluated in the assessment of neck pain

[61].

The assessment of movement, motor function, and general exercise capacity will also be required. Detailed information on the clinical assessment of cervical motor function is available elsewhere [30]. The rationale for the evaluation of such features is to plan an individualized exercise program for each patient on the basis of the assessment findings.

It is also important to gain an understanding of any psychological factors that may influence recovery or the effects of physiotherapy interventions. These are often termed “yellow flags.” Numerous psychological questionnaires are available and various psychological factors such as fear avoidance beliefs, pain catastrophizing, anxiety, and depression, among others, have been found to be relevant to neck pain [34], so it is often difficult for busy clinicians to decide on the most appropriate questionnaire/s to use. The Orebro Musculoskeletal Screening Tool was designed as a screen to identify people at risk of developing chronic pain associated with yellow flags [27]. It has been validated mostly in populations with low back pain and has moderate predictive ability in identifying patients with low back pain at risk of persisting pain and disability [22]. It has been less well researched in patients with neck pain with a recent study indicating that it may be less predictive in this patient group [11]. Physical therapy clinicians may opt to select relevant questionnaires on the basis of the patient’s history and interview. For example, if the patient reports catastrophic thoughts about their condition or circumstances, this could be further evaluated with a validated tool such as the Pain Catastrophizing Scale [63].

In the case of WAD, the precipitating event is usually a motor vehicle crash and this can be traumatic for some people. This is different to nontraumatic neck pain, which is often insidious in onset within no specific traumatic incident. It would seem to be important to take this into consideration with the assessment of patients with WAD as several studies have shown early posttraumatic stress symptoms to be associated with poor recovery following the injury [47,58,60]. Symptoms of posttraumatic stress may be suspected in patients who report difficulty sleeping due to thoughts about the accident, flashbacks, or avoidance of driving due to fear [55]. Further assessment could be undertaken using validated questionnaires such as the Impact of Events Scale recommended for use by physical therapists [38].

The physical therapy assessment of acute neck pain should consider the possible prognostic outcome of an individual patient. Is the patient at “high risk” of poor recovery or at “low risk” with encouraging signs of good recovery? Often prognostic indicators identified in cohort studies are of limited clinical use. For example, it is not clear what scores on questionnaires clinicians should

be looking for; if it is only one factor or a combination of factors that is important; and what treatment decisions should be made on the basis of the presence or not of prognostic indicators. Clinical prediction rules (CPRs) use quantitative methods to analyze the contributions of specific patient characteristics and subsequently create pathways to assist clinicians in making predictions about patient outcomes [45] or to make decisions about treatment [32]. In recent times there has been an influx of CPRs for musculoskeletal pain. For nontraumatic neck pain, various CPRs have been developed for making decisions about whether or not a patient will benefit from a specific treatment including manipulation [8], cervical traction [44], and exercise [21]. Most have been developmental studies to identify a CPR with one attempting validation in new patient cohort without success [9]. Therefore, they cannot yet be recommended for use in clinical practice. Validation of a CPR ensures that associations between given predictors and outcomes are not due primarily to chance or unique to the derivation population and is an essential step to maximize clinical utility of the tool [45]. For WAD, a CPR for predicting good and poor outcome from the acute stage of injury has been developed [47] and subsequently validated [46] (Fig. 20-1). No CPR for neck pain has yet undergone impact analysis.

MEDICAL MANAGEMENT

People with neck pain commonly seek treatment from medical practitioners, and pharmacological interventions are often prescribed with injection therapies and other invasive treatments are also used [43]. Patients also commonly see advice from physical therapists about medical management; therefore, it is important that physical therapists are aware of the current evidence base. Recent reviews of treatment for neck pain include the QTF review in 2010, the International Collaboration on Neck Pain (ICON) reviews in 2013, and Ontario Protocol for Traffic Injury Management (OPTIMa) Collaboration in 2014.

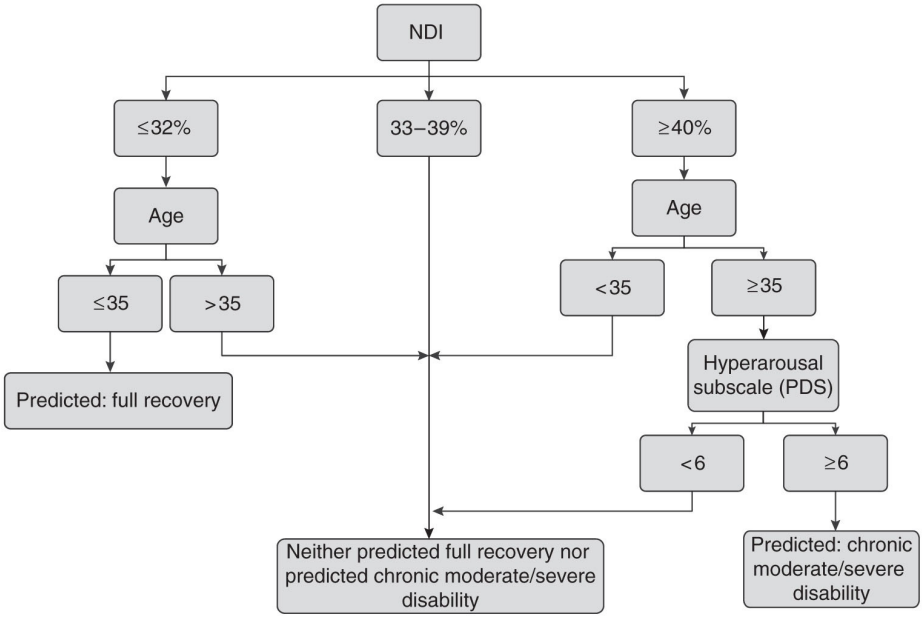

FIGURE 20-1 Whiplash CPR [46,47] to predict both chronic moderate/severe disability and full recovery following an acute whiplash injury.

Medical management commences with the patient assessment and commonly includes radiological imaging. In the case of traumatic neck pain, it has been previously discussed that the C-Spine Rule is used to determine the need for radiological imaging [37]. If required, there is strong evidence to suggest that CT scanning has superior performance to plain X-rays in the identification of cervical spine traumatic lesions [41]. In nonemergency neck pain without radiculopathy, this review concluded that the validity of most commonly used objective tests such as discography, electrophysiological evaluation, and imaging techniques is lacking [41].

Various classes of medications are commonly prescribed for neck pain including non-opioid analgesics, oral and topical nonsteroidal anti-inflammatory drugs (NSAIDs), opioids, muscle relaxants, benzodiazepines, tricyclic antidepressants, and GABA derivatives. Medicinal injections might also be used including corticosteroids, anesthetics, and neuromuscular paralytic agent (botulinum toxins). The ICON review concluded that there is a lack of evidence for most pharmacological interventions [43]. Current evidence is against botulinum toxin-A for chronic neck pain or subacute/chronic whiplash; against medial branch block with steroids for chronic facet joint pain; but in favor of the muscle relaxant eperison hydrochloride for chronic neck pain [43].

The evidence is also poor for more invasive medical interventions. The Bone and Joint Decade Task Force concluded that there is no clinical evidence to support the use of radiofrequency neurotomy for suspected zygapophyseal joint

pain [2]. This technique is controversial with some authors arguing that it is the only intervention for neck pain from the zygapophyseal joint that provides complete pain relief [1]. Carragee et al. [2] also found that cervical fusion or arthroplasty has no evidence to support their use in neck pain without radiculopathy but immediate pain relief and improved function are provided for cervical radiculopathy although whether these effects are maintained in the long term is not known. Support for short-term symptomatic improvement of cervical radicular symptoms with epidural or selective root injections with corticosteroids was found and early results from trials of cervical disc arthroplasty for radicular symptoms seem to show similar early symptomatic improvement when compared with anterior discectomy and fusion surgery [2].

PHYSICAL THERAPY INTERVENTIONS

The mainstay of management for neck pain is the provision of advice encouraging return to usual activity and exercise and this approach is advocated in current clinical guidelines [7,38] (Table 20-2 summarizes recommendations from these clinical guidelines). Various types of exercise have been investigated including range-of-movement exercises, McKenzie exercises, postural exercises, strengthening, motor control exercises, and yoga. However, the treatment effects of exercise are generally small with recent systematic reviews concluding that there is only modest evidence available supporting activity/exercise for acute WAD [48,65] and chronic neck pain in general [51]. There is no evidence that one form of exercise is superior over another [51] and this is an area that requires investigation in future studies. It is also not clear if specific exercise is more effective than general activity or merely advice to remain active [65].

Various information and educational approaches including information booklets, web sites, and videos have been investigated for their effectiveness in improving outcomes for neck pain, with the majority of trials being conducted in acute WAD [17,76]. Results suggest that patient education alone does not yield large benefits in clinical effectiveness compared with other conservative interventions for patients with neck pain with benefits being small and short lived [76]. Although patients understandably want advice on the prognosis and implications of their condition [49], it is not clear that advice per se will improve long-term outcomes or prevent chronic pain development.

TABLE 20-2 **Summary of Clinical Guideline-Recommended Treatments for Acute WAD [38] and Acute and Chronic Nontraumatic Neck Pain [7]**

Acute WAD	Nontraumatic Neck Pain
Recommended first-line treatment	Recommended—strong evidence
Assurance	Manual therapy
Advice to remain active	Co-ordination, strengthening, and stretching exercises
Neck exercises	Patient education
Simple analgesics	
NSAIDs	
May be used but weaker evidence	Recommended—moderate evidence
Manual therapy	Stretching exercises
Acupuncture	Thoracic mobilization/manipulation
Kinesiotaping	Centralization exercises
	Neural tissue mobilization
Should not be used	Recommended—weak evidence
Rest longer than 4 d	Stretching exercises
Neck collar	Thoracic mobilization/manipulation
Muscle relaxants	
Botulinum toxin type A	
Intra-articular and intrathecal steroid injections should not be prescribed	

Abbreviation: WAD, whiplash-associated disorders.

Spinal manual therapy is commonly used in the clinical management of neck pain. It is often difficult to tease out the effects of manual therapy alone as most studies have used it as part of a multimodal package of treatment. Systematic reviews of the few trials that have assessed manual therapy techniques alone conclude that manual therapy applied to the cervical spine (passive mobilization) may provide some benefit in reducing pain in WAD but that the included trials were of low quality [48,65]. In the case of chronic nontraumatic neck pain, the evidence suggests that manual (manipulation or mobilization) therapy is more - effective than no treatment, sham, or alternative interventions; however, it is not clearly superior to any other treatment in either the short or long term [26]. Physical therapy is usually delivered in a multimodal way, that is, a combination of treatments is provided. A recent systematic review of multimodal management concluded that a package including manual therapy, education, and exercise may benefit patients with neck pain [64].

Other physical modalities commonly used in the treatment of neck pain include electrotherapy, thermal treatments, acupuncture, and traction. There is moderate evidence of some short-term pain relief over placebo for acupuncture, intermittent traction, and laser for chronic neck pain but also moderate evidence of no benefit of pulsed ultrasound, infrared light, or continuous traction for acute WAD, or subacute to chronic neck pain [16]. No added benefit was found when hot packs were combined with mobilization, manipulation, or electrical muscle stimulation for chronic neck pain at 6-month follow-up [16].

In comparison with WAD and nontraumatic neck pain, very few clinical trials have investigated noninvasive physical interventions for cervical radiculopathy with a recent review concluding that on the basis of low-level to very low-level evidence, no one intervention seems to be superior or consistently more effective than other interventions [68].

PSYCHOLOGICAL TREATMENTS

In accordance with the biopsychosocial model of pain, it may be expected that physical therapy-only approaches for neck pain will not be sufficient. Few trials of psychological treatments or interdisciplinary interventions have been conducted in patients with neck pain. Of the few trials available, the tested approaches have been varied, from physiotherapists delivering psychological-type interventions in addition to physiotherapy to psychological interventions alone. In their systematic review of treatments for WAD, Teasell et al. [66] concluded that although the majority of studies suggest that interdisciplinary interventions are beneficial, it is difficult to formulate conclusions given the heterogeneity of the interventions. The ICON review notes a dearth of studies investigating psychological treatments for neck pain, especially for interventions delivered by a psychologist [18]. The conclusion of this review was that there is currently limited data available on which to inform or guide clinical practice or recommendations [18].

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CHAPTER 21

Neuropathic Pain and Complex Regional Pain Syndrome

Kathleen A. Sluka

EPIDEMIOLOGY AND DIAGNOSIS

Neuropathic Pain

Neuropathic pain is defined by the International Association for the Study of Pain (IASP) as pain that arises as a direct consequence of a lesion or disease affecting the somatosensory system (www.iasp-pain.org). Peripheral neuropathic pain is a direct consequence of a lesion or disease affecting the peripheral somatosensory system, whereas central neuropathic pain is a direct consequence of a lesion or disease affecting the central somatosensory system. Neuropathic pain can occur as a result of numerous conditions, some of which are listed in Table 21-1, and can be considered a mononeuropathy or a polyneuropathy [41]. Neuropathies, with or without pain, affect up to 8% of the population, with estimates as high as 5–7% for painful neuropathies [39]. On the other hand, 7–8% of adults with chronic pain have neuropathic symptoms. Neuropathic pain characteristics are common in a number of disease states. For example, neuropathic pain characteristics are found in 26% of people with diabetes, 37% of those attending primary care for lower back pain, 25% of those with persistent pain after surgery, and 20% of people with cancer [2,16,46]. Risk factors for development of chronic neuropathic pain are similar to that for other chronic pain conditions and include age, female sex, physical inactivity, and psychological factors such as depression, anxiety, and pain catastrophizing.

TABLE 21-1 **Origins of Neuropathic Pain**

Mononeuropathy	Polyneuropathy
Trauma—amputation, nerve injury, entrapment, neuroma, thoracotomy	*Trauma*—spinal cord injury, stroke
Other—diabetic, herpes zoster, herpes simplex, vasculitis, trigeminal neuralgia	*Metabolic or nutritional*—alcholoic, diabetic, pellegra
	Drugs—cisplatin, ethambutol, nitrofurantoin, vincristine
	Toxins—acrylamide, arsenic, ethylene oxide, pentocholorophenal, thallium
	Hereditary—amyloid neuropathy, Fabry disease, Charcot–Marie–Tooth disease
	Malignant—myeloma, carcinomatous
	Infective—Guillain–Barre syndrome, HIV

Complex Regional Pain Syndrome

Complex regional pain syndrome type I (CRPS-I, previously referred to as reflex sympathetic dystrophy) is a condition that occurs after a trauma to the distal part of the extremity such as a fracture, surgery, or sprain, and CRPS-II (also known as causalgia) occurs after direct injury to a nerve [41]. CRPS can therefore be considered as a form of peripheral neuropathic pain. CRPS-I occurs most commonly after a distal fracture; it is more common in women than men (with a 3:1 ratio), and the greatest incidence occurs between 60 and 69 years of age [11]. Incidence rates in the general population are low, with estimates of 26.2/100,000 person-years [11]. CRPS is associated with distal extremity pain and swelling, with the pain being disproportionate in time and degree to the injury. Allodynia is common in CRPS, with patients describing difficulty wearing socks or gloves. The pain, hyperalgesia, and allodynia are not related to a nerve territory. Other changes include (1) autonomic effects such as increased blood flow and sweating; (2) trophic changes such as abnormal nail growth, decreased hair growth, glossy skin, and osteoporosis; and (3) loss of range of motion, weakness, and functional motor disturbances (such as decreased proprioception, loss of fine motor control, dystonia, or tremor) [3]. The IASP diagnostic criteria [41] are outlined in Table 21-2 for types I and II. In general, CRPS-I occurs after an initiating noxious event and CRPS-II occurs after nerve injury, with the other criteria being nearly identical.

PATHOLOGY

A number of animal models have been developed to assess the pathological changes that occur after nerve injury [14,32]. These models involve injury to a peripheral nerve or to the dorsal root, lesion to the central nervous system, induction of diabetes, or delivery of chemotherapy drugs systemically [14]. In general, these models result in long-lasting mechanical and heat hyperalgesia, and decreases in function [14]. Studies using these models have identified clear alterations in the sympathetic nervous system, changes in peripheral and central glial cells, increased activity in peripheral nociceptors, and central sensitization [14,32]. Both injured and uninjured nerve fibers located within the same nerve show increased spontaneous firing, presumably as a result of upregulation of specific sodium channels ($Na_V1.3$ and $Na_V1.8$) in both injured and uninjured axons after nerve injury [13,32]. Dorsal horn neurons in the spinal cord show enhanced responsiveness to peripherally applied stimuli, including nonpainful Aβ-fiber stimuli [32,34,35]. Descending facilitation from the brainstem has been proposed to maintain the changes in the spinal cord and the hyperalgesia associated with nerve injury [5,32,36]. Thus, both peripheral and central mechanisms contribute to the pain and allodynia associated with neuropathic pain syndromes.

TABLE 21-2 Diagnostic Criteria for CRPS

CRPS-I	CRPS-II
1. Develops after an initiating noxious event	1. Develops after nerve injury
2. Spontaneous pain or allodynia/hyperalgesia occurs but is not limited to the territory of a single nerve, and is disproportionate to the inciting event	2. Spontaneous pain or allodynia/hyperalgesia occurs but is not limited to the territory of the injured nerve
3. There is or has been evidence of edema, skin blood flow abnormality, or abnormal sudomotor activity in the region of the pain since the inciting event	3. There is or has been evidence of edema, skin blood flow abnormality, or abnormal sudomotor activity in the region of the pain since the nerve injury
4. The diagnosis is excluded by the existence of conditions that would otherwise account for the degree of pain and dysfunction	4. The diagnosis is excluded by the existence of conditions that would otherwise account for the degree of pain and dysfunction

Abbreviation: CRPS-I/II, complex regional pain syndrome I/II.

The role of the sympathetic nervous system can be inferred from the results of sympathectomy (a surgical or chemical procedure that destroys nerves in the sympathetic nervous system). The sympathetic nervous system seems to play an important role in the hyperexcitability and ectopic discharges of axotomized dorsal root ganglion (DRG) neurons, because blockade of sympathetic activity decreases these discharges. Sprouting of sympathetic fibers and an upregulation of adrenergic receptors also occur in the DRG after axotomy [9,10].

Furthermore, animal studies show that sympathectomy reverses hyperalgesia in some models of neuropathic pain [19], and knockdown of $Na_V1.6$ sodium channel reduces sympathetic sprouting and hyperalgesia [51]. In some cases of clinical neuropathic pain, sympathectomy—chemical or surgical—reduces the pain and associated symptoms of neuropathic injury. However, a systematic review of the literature on chemical or surgical sympathectomy concluded that there is very little evidence to support the use of sympathectomy [42].

MEDICAL MANAGEMENT

Medical management of neuropathic pain is aimed at reducing pain and improving function through the use of pharmacological, surgical, and interventional techniques. **Pharmacological** approaches are grouped into four categories: anticonvulsants, antidepressants, opioids, and topical agents (for review see reference [43]). The anticonvulsants gabapentin (Neurontin) and pregabalin (Lyrica) reduce pain by binding to the α2δ subunit on calcium channels. Systematic reviews show that gabapentin, compared with placebo controls, is effective with at least 50% pain reduction in postherpetic neuralgia and diabetic neuropathy [27]. Other anticonvulsants (such as topiramate, levetiracetam, oxcarbazepine) have either not been tested or show limited efficacy [43,49]. The use of tricyclic antidepressants and dual reuptake inhibitors (serotonin–norepinephrine reuptake inhibitors) in the treatment of neuropathic pain has been well established [43] and is often the first treatment of choice [38]. Systematic reviews show efficacy for tricyclic antidepressants, venlafaxine, and duloxetine [25,38,43]. The use of opioids for the management of neuropathic pain is generally considered effective, but there is considerable controversy in their use for long-term pain management [43] (see Chapter 15 for more detail). As stated in *Chapter 15* there is a risk of serious side effects and addiction or abuse, and treatment of pain with strong opioids in patients with chronic nonmalignant pain should be initiated by an experienced pain specialist.

Topically administered creams such as capsaicin, lidocaine, and anti-inflammatories can also be used to manage neuropathic pain, particularly in peripheral neuropathies such as postherpetic neuralgia [43]. Topical lidocaine is more effective than placebo for reduction in pain associated with postherpetic neuralgia [12]. High-dose capsaicin cream provides a long-term effect for postherpetic neuralgia and HIV-neuropathy in randomized controlled trials (RCTs) [43].

Spinal cord stimulation is a technique in which an electrical stimulator is implanted epidurally over the dorsal column of the spinal cord and electrical current is applied (usually at 60 Hz) directly to the dorsal columns to produce an analgesic effect. Spinal cord stimulation is generally used in those who have failed conventional therapies including pharmacological and physical therapy. Several RCTs show some efficacy for spinal cord stimulation in those with failed back syndrome [22–24] (for review see reference [50]). However, Turner et al. [44] showed no evidence of effectiveness in workers compensation recipients with failed back surgery.

The use of **sympathectomy** for treatment of neuropathic pain and CRPS is historically based on the concept that the pain is "sympathetically maintained." However, a Cochrane systematic review found one study that satisfied the inclusion criteria. The study included 20 subjects that compared two forms of sympathectomy and showed a positive reduction in pain in both groups. They conclude there is "very little high-quality evidence" for the practice of sympathectomy for neuropathic pain and CRPS and should be used cautiously and only after failure of other treatment options [42].

In summary, there is good evidence for the use of systemically administered antidepressants and anticonvulsants, and for the use of topical capsaicin and lidocaine for patients with neuropathic pain. There is also evidence for the use of spinal cord stimulation for the treatment of neuropathic pain and CRPS. However, there is limited evidence for sympathectomy for the management of neuropathic pain and CRPS.

PSYCHOLOGICAL MANAGEMENT

There is limited evidence for the efficacy of psychological treatment in neuropathic pain, despite its common use in patients with painful neuropathic disorders [48]. The systematic review by Wetering et al. [48] found 14 studies and 3 RCTs and the rest were controlled and uncontrolled trials. One of these studies had good methodological quality and showed a significant effect but only in females. Despite this, chronic pain conditions in general respond well to psychological interventions, including cognitive-behavioral therapy, relaxation, and education on coping skills (see Chapter 13).

PHYSICAL THERAPY MANAGEMENT

Evidence for effectiveness of physical therapy treatments for neuropathic pain conditions, including CRPS, is limited, particularly with respect to high-quality RCTs (Table 21-3) [30]. However, treatments usually involve the use of (1) exercise therapy to improve range of motion, strength, and coordination; (2) sensory and motor reeducation to improve pain and improve function; (3) modalities such as transcutaneous electrical nerve stimulation (TENS) to reduce pain; and (4) graded motor imagery and mirror therapy (for review see reference [15]).

Exercise therapy should be used to improve and restore function in patients with neuropathic pain. Several studies include exercise as part of the protocol for treatment of neuropathic pain. However, there is a general lack of RCTs evaluating the effectiveness of physical therapy for acute or chronic neuropathic pain conditions other than CRPS. In one study in people with diabetic neuropathy, however, a 10-week aerobic and strengthening program exercise reduced pain and neuropathic symptoms and improved intraepidermal nerve fiber branching [20].

TABLE 21-3 **Evidence for Physical Therapy Treatments of Neuropathic Pain and CRPS-I/II**

Treatment	Type of Study	Results
Exercise	RCT, CT, case series	Reduces pain at rest and with movement, improves range of motion, improves function
TENS	RCT	Reduces pain and allodynia
Motor imagery/ mirror therapy	RCT	Reduces pain, analgesic consumption, swelling, and disability
Desensitization therapy	Systematic review based on an RCT	Reduces allodynia and improves hand sensibility

Abbreviations: CRPS-I/II, complex regional pain syndrome type I/II; TENS, transcutaneous electrical nerve stimulation, RCT, randomized controlled trials.

The literature evaluating the effects of exercise for acute or chronic CRPS includes a few controlled trials, some of which were randomized to other treatments for comparison. For adults with CRPS-I, a controlled trial was performed involving a stress-loading program of scrubbing, carrying, and functional hand-loading activities. The program results in a decrease in pain and trophic changes and improvements in grip strength and range of motion [47]. For children with CRPS, an uncontrolled study found that exercise results in a complete resolution of pain and return of function in nearly all patients [40]. However, in the above studies, there was no control comparison group, and thus subjects were not randomized. When physical therapy, defined as exercise using graded activity to improve function, strength, and mobility, is combined with

spinal cord stimulation in patients with chronic CRPS, there is no difference compared with a group that only received spinal cord stimulation [17]. However, all patients had received prior physical therapy, and a large number of patients (approximately 50%) did not complete the study, mostly because of a change in treatment plan by the therapist or because of a worsening condition. These problems make it difficult to draw any conclusions of effectiveness in this study. In another study of acute CRPS of the upper extremity, physical therapy was compared with occupational therapy, and a control condition that included education and social work. The experimenter selected treatments on the basis of the following objectives: physical therapy objectives were to increase pain control, optimize coping skills, and extinguish the source of pain, and occupational therapy objectives were to reduce inflammation, protect and support the hands, normalize sensation, improve hand function, and improve activities of daily living. Physical therapy improved pain, both at rest and with movement, and increased range of motion of the upper extremity to a greater extent than occupational therapy or the control condition [31]. A recent single-case design study used an aggressive progressive loading exercise program, termed pain exposure, in people with chronic CRPS-I and show improvements in pain, strength, disability, kinesophobia, and quality of life [45]. Although exercise is recommended in treatment guidelines, future studies need to evaluate effectiveness and dosing of exercise in RCTs in those with neuropathic pain and complex regional pain.

TENS, when used for treatment of neuropathic pain, is typically applied either over the affected nerve, or if the pain is too severe for the patient to tolerate direct stimulation, the electrodes can be placed around the painful area. High-frequency TENS, assessed in RCTs, reduces pain in people with diabetic neuropathy, mixed peripheral neuropathies, and spinal cord injury [1,6,8,18,21]. These studies show reductions in both resting pain and allodynia when compared with placebo. Thus, there is good evidence from RCTs that TENS is effective in patients with neuropathic pain.

Motor imagery and mirror feedback exercises have been assessed in people with neuropathic pain and CRPS. Mirror therapy involves movement of the affected limb inside a mirror box to provide visual feedback of the affected hand to replace that of the (reflected) unaffected hand. Pain is reduced in people with acute or chronic CRPS-I following treatment with mirror therapy in RCTs when compared with standard treatment and has been confirmed in a recent systematic review [4,26,28,29]. Graded motor imagery extends mirror therapy by providing training in recognition of lateralization and visualizing movements in addition to mirror therapy [28,29]. The systematic review shows weak

evidence that mirror therapy and graded motor imagery are more effective for reducing pain than the control treatment [4]. This technique is similarly effective for patients with phantom limb pain [7,37]. Thus, there is evidence from RCTs that motor imagery using mirror therapy reduces pain and disability in people with CRPS-I and phantom limb pain.

Similarly, graded sensory stimuli are often used to extinguish the allodynia associated with CRPS. **Sensory reeducation**, also referred to as desensitization therapy, relies on controlled stimuli aimed at desensitizing the affected limb. Graded stimuli are applied to the allodynic area of the affected limb starting with soft stimuli, such as a cotton wisp, and increasing to a rough stimulus, such as sandpaper. Kits can be purchased through hand therapy catalogs and include graded textures that are rubbed on the skin, or buckets of graded sensory particles in which the limb can be placed. One high-quality RCT supports the use of sensory reeducation for people with neuropathic pain to reduce allodynia and improve cutaneous sensibility [33].

In summary, there is weak evidence from controlled trials, both randomized and nonrandomized, to support the use of exercise for treatment of neuropathic pain and CRPS. Despite this, exercise is highly utilized in people with neuropathic pain conditions and generally recommended in consensus-based clinical practice guidelines. There is good evidence to support the use of TENS and mirror image therapy for neuropathic pain and CRPS and limited evidence to support the use of sensory reeducation therapy for CRPS.

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CHAPTER 22

Osteoarthritis and Rheumatoid Arthritis

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EPIDEMIOLOGY AND DIAGNOSIS

Arthritic conditions can generally be classified into inflammatory or noninflammatory conditions. Inflammatory conditions are the least prevalent with rheumatoid arthritis (RA) affecting approximately 1% of the population [13,30]. On the other hand, the prevalence of osteoarthritis (OA) and degenerative joint disease increases with age reaching approximately 50% of those over the age of 65 [30]. This chapter will focus on RA and OA as they are commonly treated by physical therapists. Both RA and OA are more common in women than men, and women with OA have higher pain and worse function [48,52].

DIAGNOSTIC CRITERIA

Osteoarthritis

Degenerative joint disease is a chronic disease that affects the cartilage and subchondral bone. There is a loss of articular cartilage, new bone, and cartilage formation, which is generally confirmed by radiological criteria. The severity of OA by radiograph is scored on the Kellgren–Lawrence scale: 0, no features of OA; 1, doubtful OA with minute osteophytes; 2, minimal OA with definite osteophytes but unimpaired joint space; 3, moderate OA with osteophytes and moderate loss of joint space; and 4, severe OA with greatly impaired joint space and sclerosis of subchondral bone [30]. Diagnostic criteria by the American College of Rheumatology combine symptoms with radiographic evidence of joint destruction [2]. Diagnostic criteria for primary OA are outlined in Table 22-1 with “3” reflecting the criteria for the knee. Although OA is traditionally

thought to be noninflammatory, there is evidence that there is a mild inflammation of the synovium [30,48]. OA is associated with pain, stiffness, functional limitations, and decreased quality of life [30]. Localized OA generally occurs in the knees or hips but can also occur in other joints such as the hand and shoulder. OA can also be generalized occurring in multiple joints (i.e., knees, hips, and hands). Pain is the major reason an individual seeks medical attention and is the major determinant of functional loss and decreased quality of life in people with OA.

Pain with OA is generally worse with activity and use of the joint, which leads to the decreased function in these individuals. Oftentimes, the radiographic evidence does not match the severity of pain [48]. Furthermore, women have greater pain and worse function with the same level of radiographic evidence in those with OA of the knee [52]. Recent reviews examine the underlying pathology of the cartilage, biomechanics, and neural changes in OA and how this pertains to sex differences [9,31,48]. Pain in people with OA has been extensively studied. Despite clear peripheral changes, there are signs of alterations in central processing with individuals with OA showing higher levels of temporal summation, a measure of central pain excitability, than healthy controls, and those with the greatest levels of pain (>6/10) showing more temporal summation than those with lower levels of pain [3]. Further, there is less-conditioned pain modulation, a measure of central inhibition, in those with OA. In addition, certain psychosocial factors can enhance the pain experience, and are associated with poor response to treatment [48]. These include pain catastrophizing, anxiety, depression, fear of movement, and poor social support. Predictors of poor outcome following total knee replacement have also been investigated and include pain during knee flexion prior to surgery, anxiety, and depression [33,35,48].

TABLE 22-1 Diagnostic Criteria for Primary OA (American College of Rheumatology)

1. Localized
   a. Hip
   b. Knee
   c. Hand
   d. Other, shoulder, elbow, wrist, ankle
2. Generalized: multiple joints
3. Pain and five of the following criteria
   a. Age >50 y
   b. Stiffness <30 min
   c. Crepitus
   d. Bony tenderness
   e. Bony enlargement
   f. No palpable warmth
   g. ESR <40 mm/h
   h. Rheumatoid factor < 1:40
   i. Synovial fluid signs of OA
   j. Osteophytes

Abbreviations: OA, osteoarthritis; ESR, erythrocyte sedimentation rate.

Rheumatoid Arthritis

RA is an autoimmune disease associated with chronic inflammatory polyarthritis affecting multiple joints usually in a symmetrical pattern [30]. The cause of RA is unknown but likely involves both genetic and environmental factors [30]. Inflammatory synovitis is the key pathological feature in RA and results in inflammatory cell infiltration and hypertrophy of the synovium. There is increased production of tumor necrosis factor alpha (TNF-α) and interleukin-1, as well as destructive enzymes (i.e., matrix metalloproteinase enzymes) produced by the synoviocytes [30]. In addition to joint inflammatory signs, there are signs of fatigue and 20–40% of people with RA have signs of systemic disease outside the joint including pulmonary, cardiac, or vascular, ocular, and neurological symptoms [30]. Laboratory findings include abnormal X-ray showing soft tissue swelling, loss of joint space, bony erosions; abnormal erythrocyte sedimentation rates (ESRs); and a positive serum rheumatic factor [30]. However, it should be noted that a portion of those with RA do not test positive for rheumatoid factor or other markers—referred to as seronegative RA. General criteria for diagnosis are outlined in Table 22-2 and based off the 2010 classification proposed by the American College of Rheumatology [1,30].

TABLE 22-2 The 2010 American College of Rheumatology/European League against Rheumatism Classification Criteria for RA

Score
Target population (who should be tested?): Patients who
1. have at least 1 joint with definite clinical synovitis (swelling)*
2. with the synovitis not better explained by another disease†
Classification criteria for RA (score-based algorithm: add score of categories A–D; a score of >6/10 is needed for classification of a patient as having definite RA)
A. Joint involvement§
1 large joint—0
2–10 large joints—1
1–3 small joints (with or without involvement of large joints)—2
4–10 small joints (with or without involvement of large joints)—3
>10 joints (at least 1 small joint)**—5
B. Serology (at least 1 test result is needed for classification)††
Negative RF *and* negative ACPA—0
Low-positive RF *or* low-positive ACPA—2
High-positive RF *or* high-positive ACPA—3
C. Acute-phase reactants (at least 1 test result is needed for classification)
Normal CRP *and* normal ESR—0
Abnormal CRP *or* abnormal ESR—1
D. Duration of symptoms
<6 wk—0
>6 wk—1

*The criteria are aimed at classification of newly presenting patients. In addition, patients with erosive disease typical of rheumatoid arthritis (RA) or previously classified as having RA with a history compatible with prior fulfillment of the 2010 criteria should be classified as having RA.

†Differential diagnoses vary among patients with different presentations, but may include conditions such as systemic lupus erythematosus, psoriatic arthritis, and gout.

§Joint involvement refers to any *swollen* or *tender* joint on examination, which may be confirmed by imaging evidence of synovitis. Large joints refer to shoulders, elbows, hips, knees, and ankles. Small joints refer to the metacarpophalangeal joints, proximal interphalangeal joints, second through fifth metatarsophalangeal joints, thumb interphalangeal joints, and wrists.

**In this category, at least 1 of the involved joints must be a small joint; the other joints can include any combination of large and additional small joints, as well as other joints not specifically listed elsewhere (e.g., temporomandibular, acromioclavicular, sternoclavicular, etc.).

††Negative refers to values that are less than or equal to the upper limit of normal (ULN); low-positive refers to values that are higher than the ULN but ≤3 times the ULN; high-positive refers to values that are >3 times the ULN.

Abbreviations: ACPA, anti-citrullinated protein antibody; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate.

RA has a distinctly different pain pattern than OA. In general, inflammatory conditions like RA are worse with rest and result in stiffness in the morning lasting greater than 1 hour, get better with low-grade activity, and are associated with swelling. In contrast, people with OA are generally better with rest, get progressively worse throughout the day with activity, and have minimal signs of inflammation [30].

PATHOLOGY

Osteoarthritis

OA is associated with loss of cartilage, remodeling of bone, and intermittent inflammation [30,48]. There are changes in the synovium, bone, and ligaments that begin early in the process and are primarily associated with activity-related pain [30]. Cartilage degradation is a hallmark of OA, and this damage may be responsible for the pain with movement due to mechanical activation of nociceptors innervating the subchondral bone [48,51]. Indeed, there is sprouting of nerve fibers to joint tissues not previously innervated particularly into subchondral bone [51]. The synovium can become inflamed and there is release of inflammatory cytokines such as inerleukin-1 and TNF from chondrocytes, and synoviocytes contribute to the cartilage destruction [48]. These inflammatory substances released into OA joints sensitize peripheral nociceptors and lead to central sensitization of dorsal horn neurons [44]. There is also a loss of inhibitory control mechanisms in people with OA [27], and enhanced temporal summation [3]. Together, the peripheral and central changes observed in people with OA contribute to the pain and loss of function.

Rheumatoid Arthritis

RA is an inflammatory joint disease with synovitis as the key feature textbook of pain [30]. Associated with the disease are inflammatory cell infiltration into the joint and joint tissues that results in hyperplasia of the synovial lining, fibrin deposition, and joint destruction. Basic science research has resulted in a good understanding of the cellular and molecular events that occur in joint tissue in inflammatory joint disease, which have resulted in production of multiple potential treatments aimed at modifying the disease mechanisms. Activated synoviocytes are the major source of inflammatory mediators and proteinases. Synoviocytes release multiple inflammatory cytokines, including TNF-α, interleukin-1, and interleukin-6, and have been measured in synovial fluid from people with RA [30]. Metalloproteinases and other destructive enzymes are also released and result in cartilage damage [30]. As noted below, targeting effects of TNF-α and interleukin-1 and other cellular pathways have become standard of care.

ASSESSMENT CONSIDERATIONS

Special considerations for the assessment of pain in people with OA and RA include analyzing the nature of the pain across the day, assessment of pain with functional activities, and assessment of the impact of pain on daily function. The Knee Injury and Osteoarthritis Outcome Score (KOOS) was developed as an extension to the Western Ontario and McMaster Osteoarthritis Index (WOMAC) and includes the WOMAC as part of the assay. The KOOS and WOMAC are commonly used for people with OA to assess the impact of pain on function and have proven valid and reliable [5,41]. For RA, assessments should also include examining for signs of inflammation, swelling, stiffness, and pain, in multiple joints. Disease activity in RA is assessed by taking into account joint swelling and tenderness, pain, and function. Sometimes this is done with a disease activity score derived from a 28-joint count (DAS28). Additionally, assessment of pain in RA might include standard pain scales, self-efficacy questionnaires, quality-of-life questionnaires, and measurement of functional deficits. Developed by the same group who developed the KOOS there is questionnaire aimed at people with rheumatoid and OA of the lower extremities: Rheumatoid and Arthritis Outcome Score (RAOS) [41]. Both the KOOS and RAOS are available and free for use from their website (www.koos.nu).

MEDICAL MANAGEMENT

Management of OA and RA requires a multidisciplinary approach that includes pharmacology, psychology, physical therapy, and surgery. Treatment of people with OA is generally aimed at managing symptoms (i.e., pain) and improving functional capacity. On the other hand, treatment of RA uses disease-modifying drugs and anti-inflammatory medications to reduce disease process and the accompanying symptoms.

Osteoarthritis

The goals for medical management of OA are to reduce the pain and symptoms either through systemic pharmacological treatments, or local intra-articular injections. The American College of Rheumatology and Osteoarthritis Research Society International (OARSI) have developed evidenced-based guidelines for the management of OA with pharmacological treatments [20,56,57] (Table 22-3). Use of nonsteroidal anti-inflammatory drugs (NSAIDs), tramadol, and topical capsaicin are recommended. Systematic reviews show that opioid agonists

(tramadol), acetaminophen, and NSAIDs reduce pain and in some cases improve function in people with OA [14,16,53]. Effects of opioids were small (<1/10), and are contrasted by the increased risk of adverse events [16]. Local treatments generally include intra-articular injection of corticosteroids or hyaluronic acid. Intra-articular corticosteroid injection is more effective than placebo for pain reduction and global assessment by patients producing decreases in pain for up to 4 weeks [6]. Furthermore, intra-articular injection of hyaluronic acid is more effective than corticosteroids for changes in pain, WOMAC, and range of motion [6], and is recommended in guidelines. Additional nonpharmacological approaches recommended in guidelines include weight loss, exercise, joint protection techniques, and thermal modalities [20]. Total joint replacement is considered when pain and functional limitations result in a diminished quality of life, there is radiographic evidence of joint damage, and there is moderate to severe pain that is not adequately relieved by nonsurgical approaches [32]. Total joint replacement, generally of the hip and knee, is the primary surgical approach and it clearly reduces pain and improves function and quality of life in people with OA as confirmed by the National Institutes of Health (NIH) consensus statement. According to the consensus statement there is a rapid and substantial improvement in the patient's pain, functional status, and overall health-related quality of life in about 90% of patients; about 85% of patients are satisfied with the results of surgery [32].

TABLE 22-3 **Evidence for Physical Therapy Treatments for OA**

Treatment	Pain	Function
Aerobic exercise	+ (Systematic review)	+ (Systematic review)
Strengthening exercise	+ (Systematic review)	+ (Systematic review)
TENS	? (Systematic review)	Not examined
Cryotherapy	? (Systematic review)	? (Systematic review)
Heat therapy	? (Systematic review) Note: recommended	Not examined
Ultrasound	+ (Systematic review)	Not examined

Abbreviation: TENS, transcutaneous electrical nerve stimulation.

Rheumatoid Arthritis

RA management has undergone significant changes in the last 20–30 years from a focus on symptomatic relief to a treat-to-target approach using combinations of disease-modifying antirheumatic drugs (DMARDs), including biologics, and there are published guidelines from the American College of Rheumatology and the EULAR [46,50]. Early recognition and treatment with DMARDs are

important to achieve control of the disease and prevent joint injury and disability. The goals of therapy are therefore to reduce or eliminate joint pain and swelling, prevent joint damage, and minimize functional limitations and disability (Table 22-4). DMARDs are drugs that have a beneficial effect on the course of RA by slowing the progression of the disease. They also decrease symptoms such as pain and swelling, and improve function and quality of life. Common DMARDs include methotrexate, hydroxychloroquine, and sulfasalazine. Newer DMARDs are referred to as biologics and include agents aimed at reducing TNF-α effects (e.g., enteracept, adalimumab, infliximab), which are the first-line choice for biologics. Other biologics are used if TNF inhibitors are not effective and include agents aimed at blocking interleukin-1 (e.g., anakinra) or interleukin-6 (tocilizumab), blocking T-cell activation (abatacept), and inhibiting B cells (e.g., rituximab). The effectiveness of these DMARDs has been confirmed in numerous systematic reviews and meta-analyses and generally shows that combinations of DMARDs are more effective than monotherapy in halting disease progression [24,29,34,45,47] and thus should be utilized for all patients with RA. Drugs aimed at reducing the inflammatory process are utilized as analgesics and to relieve inflammation. Corticosteroids and NSAIDs can be used to reduce symptoms as an adjunct to DMARDs. For relief of pain, acetaminophen is also an effective treatment producing similar results to that of NSAIDs [30].

TABLE 22-4 **Evidence for Physical Therapy Treatments for RA**

Treatment	Pain	Function
Aerobic exercise	+ (Systematic review)	+ (Systematic review)
Strengthening exercise	+ (Systematic review)	+ (Systematic review)
TENS	+ (Systematic review)	Not examined
Cryotherapy	? (Systematic review)	– (Systematic review)
Superficial heat therapy	? (Systematic review)	Not examined

Abbreviations: RA, rheumatoid arthritis; TENS, transcutaneous electrical nerve stimulation.

PSYCHOLOGICAL MANAGEMENT

OA and RA are chronic illnesses with significant impact on quality of life. Although they are clearly associated with peripheral tissue damage, the pain and loss of function in individuals with OA and RA impact quality of life. As such, cognitive behavioral approaches are aimed at teaching coping skills and preventing fear of further injury. Cognitive-behavioral therapy for people with

RA reduces pain and joint counts, and it improves self-efficacy (for review see references [54,55]). Cognitive-behavioral therapies have typically utilized coping strategies, relaxation therapy, education on disease and treatments, and stress management skills. When compared with routine care, people with RA show improvements in pain affect, coping, and emotional stability [54,55]. Long-term effects of cognitive-behavioral therapy are observed for at least 12–15 months after treatment as evidenced by decreased usage of medical service and reductions in pain [10,26,55]. Mindfulness also shows a reduction in disease severity, including the number of affected joints, pain, and stiffness, in RA, when compared with a no-treatment control [17]. Similarly, in people with OA, cognitive-behavioral therapy reduces pain and effects are maintained through a 6-month follow-up. Sessions are effective given individually, groups, or over the Internet [10,25,26,38]. Furthermore, physical therapists can be trained to deliver a high-quality pain-coping skills program and thus may be a method of adding psychological coping skills training to clinical practice [12].

PHYSICAL THERAPY MANAGEMENT

The goals of physical therapy management of OA and RA are to maintain or improve function, and decrease pain. Exercises, both aerobic and strengthening programs, work to improve function and along with other modalities decrease pain. Because RA has a strong inflammatory component, treatment with anti-inflammatory modalities, such as ice, is also beneficial. Education is also a key component to treatment of both conditions focusing on the disease process, the benefits of routine physical exercise, and home management of pain with heat and ice modalities.

Osteoarthritis

The American College of Rheumatology and OARSI have developed evidence-based guidelines for the management of OA with nonpharmacological treatments [20,56,57]. Physical therapy interventions include those aimed at reducing pain (i.e., transcutaneous electrical nerve stimulation [TENS] and thermotherapy) and those aimed at improving function and pain (i.e., exercise). In fact, there is good evidence that either land-based or aquatic **exercise** reduces pain and improves physical function for people with OA [4,18,19] and is strongly recommended in clinical practice guidelines [20,56,57]. In a meta-analysis, both aerobic and

strengthening exercises are effective in reducing pain and decreasing disability in people with OA [40]. Recommendations from systematic reviews and evidence-based practice guidelines suggest that effective exercise programs should include advice and education to promote increased physical activity [20,40,56,57]. A recent pilot study showed that an intervention that combines pain-coping skills training with exercise can be delivered by specially trained physical therapists and results in improvement in physical and psychological outcomes in people with OA [21]. Larger clinical trials are currently underway [7,36].

For physical therapy management of pain in people with OA, a number of **electrophysical agents** show effectiveness for reducing pain and/or improving function. The effect of **TENS** for osteoarthritic pain is controversial with some systematic reviews showing effectiveness and others showing no effect [8,43]. It is possible that the differences may be related to intensity of application of TENS as Bjordal and colleagues [8] show effectiveness with adequate dosage when compared with those without, and this has been reviewed in Chapter 11 and prior reviews [49]. Other recommended adjunct therapies include **heat** and **cold** therapy, **ultrasound**, and **laser** therapy [42]. Cochrane systematic reviews show support for ultrasound in hip or knee OA, and clinical practice guidelines conditionally recommend the use of heat and cold therapy, joint protection techniques, and assistive devices [20].

In summary, the main physical therapy intervention for those with OA is to establish an exercise program and there is strong evidence to support its effectiveness. Combining psychological interventions with special physical therapy training or with training by psychologists may improve outcomes and exercise adherence. Additional pain-relieving modalities may be helpful to reduce pain to allow patients to participate in an exercise program.

Rheumatoid Arthritis

The goals for people with RA are to improve or maintain function and reduce pain. Patient **education** reduces disability, joint counts, global assessment, and psychological status in people with RA [37]. Education in people with RA can increase compliance with an exercise program, but effects are of short term [28].

Exercise is recommended to improve function, decrease fatigue, and decrease pain in RA; this has been extensively reviewed [15] and is part of practice guidelines [23]. In fact, Hurkmans and colleagues [22] in a systematic review published by the Cochrane Collaboration recommend a combination of strengthening programs and aerobic exercises for individuals with RA on the

basis of moderate-level evidence from high-quality clinical trials. No concerns were found with respect to safety and there were no deleterious effects, such as increased pain or joint damage, with exercise in the included studies. In fact, high-intensity resistance exercise is safe and can increase lean body mass, reduce fat mass, and improve muscle strength and physical function [15]. Notably, exercise reduces pain, improves morning stiffness, reduces fatigue, and does not exacerbate disease activity.

Additional physiotherapy treatments may be used to help control pain and include TENS, heat, and cold modalities. The use of electrical stimulation (i.e., **TENS**) significantly improves hand function, pain at rest, joint tenderness, and patient assessment of joint pain, but not pain with grip when compared with a placebo or no-treatment controls [11]. The use of thermal modalities for the treatment of pain in people with RA has minimal data from relatively low-quality randomized controlled trials to support its use. Although no significant effects or superficial **heat** or **cold** therapy is observed in people with RA for pain, range of motion, or function, thermal modalities are recommended as a palliative therapy [39]. At present, there is no data on **manual therapy** techniques to support or refute their effectiveness in RA. In summary, evidence suggests that relief of pain can be accomplished with a number of nonpharmacological treatments including exercise, TENS, and thermal therapy. Furthermore, improved function can be accomplished with strengthening and aerobic exercises, which are the recommended treatments.

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CHAPTER 23

Pain Associated with Central Nervous System Disorders: Central Neuropathic Pain

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Central neuropathic pain is defined as pain caused by a direct lesion or disease affecting the somatosensory system in central nervous system (CNS) [60]. Various lesions can induce central pain (listed in Table 23-1), the most common of which are spinal cord injury (SCI), stroke, and multiple sclerosis (MS) [17,67]. Although the lesion may occur at any level along the neuroaxis (from the spinal cord to cerebral cortex), central neuropathic pain conditions share common clinical features that include partial or complete loss of sensation to one or more modalities, and the development of hypersensitivity in body regions that have lost normal somatosensory information as a result of the CNS lesion [62]. The onset of pain may be immediate or significantly delayed for weeks and months after the lesion, often resulting in persistent long-lasting chronic pain. Because many central lesions have a significant effect on motor function, pain is often neglected by clinicians despite the significant impact on the patient's quality of life [64]. Adding to the complexity of central pain conditions is the fact that not all types of pain in these patients can be attributed to a specific disorder of the somatosensory system [92,103,115]; and other clinical features of their disorder such as headaches, spasticity, sleep disturbances, cognitive impairments, and musculoskeletal pain may either give rise to pain or exacerbate the neuropathic condition.

As central neuropathic pain is associated with a heterogeneous group of diagnosis, this chapter will focus on describing the most common causes of central pain, namely pain associated with SCI, stroke, MS, and Parkinson disease (PD).

EPIDEMIOLOGY AND DIAGNOSIS

Central neuropathic pain may be further defined as stimulus evoked or stimulus independent. Stimulus-evoked pain may include hyperalgesia and allodynia with hypersensitivity to mechanical, thermal, or chemical stimulation. Stimulus-independent pain, often categorized as ongoing or spontaneous pain, may be persistent or paroxysmal and descriptors such as shooting, stabbing, or burning may be used [40].

The incidence and prevalence of central neuropathic pain are not well established in all central neuropathic pain disorders. A consistent definition of central neuropathic pain needs to be utilized throughout health care systems and epidemiological studies to further clarify incidence and prevalence in this population. In addition, because of the association of central pain to a medical diagnosis such as SCI, traumatic brain injury (TBI), stroke, MS, or PD, the central neuropathic pain may be underreported.

TABLE 23-1 Common Causes of Central Pain and Prevalence

Lesion/Disease	Overall Population with Lesion/Disease (%)	Patients with Lesion/Disease and Central Neuropathic Pain (%)
SCI	8.8% of the population [88]	Greater than 50% of SCI patients develop neuropathic pain within the first 6 mo postinjury Up to 75% develop neuropathic symptoms 5 y postinjury [103]
Traumatic brain injury	8.3% of the population [28]	Chronic headache 59%; more studies needed for central neuropathic pain
Stroke	2.8% of the population [48]	4.5–7.3% CPSP; 8.3% CPSP with dysesthesia or pain [68]
MS	1.4% of the population [87]	Approximately 26% [44]
PD	0.1–0.3% of the population [114]	36% paresthesia/neuropathic pain [97]

Abbreviations: CPSP, central poststroke pain; MS, multiple scoliosis; SCI, spinal cord injury; PD, Parkinson disease.

Central Pain Post–Spinal Cord Injury

The International Spinal Cord Injury Pain System (ISCIP) [60,104] classifies pain into three tiers in SCI: (1) nociceptive pain; (2) neuropathic; or (3) other. Nociceptive pain incorporates musculoskeletal pain, visceral, and other. For neuropathic pain, three tiers are also identified: (1) at-level of SCI; (2) below-level of SCI; or (3) other. Further characterization of neuropathic pain includes (1) cauda equina or syringomyelia; (2) spinal cord lesion; or (3) postthoracotomy [21,25,117,118].

It is estimated that more than 50% of SCI patients develop neuropathic pain within the first 6 months after injury, and up to 75% develop neuropathic symptoms 5 years after injury [5,6,42,102]. Importantly, approximately one-third

of these patients report their pain as severe [75]. At-level neuropathic pain was present in 41% and below-level neuropathic pain in 34% [103]. Recent studies suggest that those who experience early sensory hypersensitivity are at risk of developing long-standing central pain following SCI and stroke [43,69,103].

Posttraumatic Brain Injury

Chronic pain in post-TBI develops from 2 weeks to 30 months after injury [93]. The prevalence of chronic pain in post-TBI ranges from 22% to 95% of patients [2,12,73,109]. Chronic pain in this population is often categorized as nociceptive, neuropathic, or headache, similar to that for SCI. Chronic pain after TBI occurs throughout the body with the head being the most common area (59%) [85]. Central pain post-TBI has been documented in case reports [65] but is less well documented for epidemiologic comparisons.

Poststroke Pain

Central neuropathic pain in the poststroke population typically occurs in the areas associated with a loss of sensory innervation in the body. Onset of pain after stroke occurs within 1–6 months [116]. Pain after stroke is divided into three categories: (1) nociceptive (subluxation of the glenohumeral joint, rotator cuff tear, or soft tissue injury); (2) central neuropathic pain; or (3) headache. It is estimated that 2–8% of patients experience central pain after stroke [20,74].

Multiple Sclerosis

Pain is a common symptom in patients with MS with prevalence of 50–85% [3,59,84,106,110]. For example, Osterberg, in a sample of 364 patients, described pain in 57% of patients, with 21% nociceptive, 2% peripheral neuropathic, 1% spasticity related, and 23.5% central pain [94].

Parkinson Disease

Estimates of pain in PD can range from 30% to 85% [33,38,45,97]. Types of pain in PD have been described as musculoskeletal, radicular-neuropathic, dystonic pain, central neuropathic pain, and akathisia or related to restless leg [13,33]. In a study by Beiske et al. [13], pain was reported in 83% of patients, with patients reporting as few as one pain type (53%), two pain types (24%), and

three pain types (5%). Central neuropathic pain was reported by 10% [13]. Pain was not associated with age, disease duration, or severity of disease. Female gender was the only predictor of pain in PD.

PATHOLOGY

The etiologies associated with the development of central pain vary greatly in structure, size, and location of the lesion. The quality of the pain also differs significantly among patients with similar lesions and between the various causes. It is therefore unlikely that a single mechanism explains all aspects and complexities surrounding central pain. Several theories have been proposed as mechanisms in the development of central pain. Common pathophysiological features in central pain include disinhibition, sensitization, and neuroplasticity alterations (reviewed in reference [63]) (see Chapters 2 and 3). In general, central pain and hyperexcitability experienced results from increased neuronal activity and neuronal reactivity and reduced inhibitory mechanisms that lead to central sensitization and disinhibition of pain pathways [17,125].

Experimental models and clinical studies demonstrate a number of central pathophysiological processes including the presence of sensitization of second- and third-order neurons in the CNS that contribute to the development and maintenance of central pain [41]. Loss of ascending input into the lateral, ventral posterolateral, and medial thalamic nuclei have all been associated with the development of central poststroke pain [16,66]. Animal studies support these findings showing that spinothalamic tract lesions in the spinal cord induce thalamic hyperexcitability that results in central pain [112]. In this model, treatment with a calcium-channel blocker reduces thalamic hyperexcitability and attenuates spinal injury–induced pain [113]. These data support that lesions of the thalamus (poststroke) and thalamic input pathways (spinal cord) contribute to thalamic sensitization and central pain.

Several mechanisms may trigger and maintain hyperexcitability following injury including the increased release of excitatory amino acids, loss of inhibition from γ-aminobutyric acid (GABA)-containing neurons, and increased descending facilitation [39] (see Chapter 3). The use of experimental models, particularly SCI models, has led to a better understanding of the cellular and molecular mechanisms of central pain. Numerous cellular processes have been implicated as a “central cascade” of interrelated events to trigger the development of central pain [123]. These components include excitotoxic,

neurochemical, anatomical, and inflammatory events that act together to drive physiological alterations in spinal and supraspinal neurons [124]. Well-documented initial consequences following stroke, traumatic brain injury, and SCI include the release of toxic levels of neurotransmitters, such as glutamate. Excessive release of glutamate not only causes neuronal death, but also activates signaling cascades to initiate inflammatory responses and cellular transcription that impact anatomical and functional properties of neurons contributing to the development of central pain [49,98].

Recently, there has been increased attention on inflammatory contributions to neuronal hyperexcitability and central pain generation [70,111,127,128]. There is evidence of widespread activation (spinal and supraspinal) of microglia and the release of pro-inflammatory substances that contribute to the development of central neuropathic pain in MS and following SCI [1,56]. Several studies conducted in SCI animals models demonstrate that interventions targeted at inhibiting inflammation are effective to reduce pain-like behaviors in SCI models [111]. There is also mounting evidence that increased sodium-channel expression drives central neuropathic pain [52,53,122]. Specifically, changes in sodium channels ($Na_v1.3$ and $Na_v1.8$) have been identified at points throughout the neuraxis including primary afferent fibers (i.e., nociceptors), spinal cord, and thalamus [53,122].

Central neuropathic pain was once widely presumed to be maintained entirely by central mechanisms. However, recent efforts provide evidence to support peripheral contributions in the development of central pain. Studies using animal models show that primary afferent neurons contribute to the development of pain following SCI. These studies show that SCI triggers chronic hyperexcitability, spontaneous activity, and enhanced intrinsic growth of primary afferent fibers, and blocking these injury-induced afferent responses prevents development of SCI-evoked pain and spontaneous dysesthesias [7,8,10,11,122]. These findings support that shared pathophysiological features exist between central and peripheral neuropathic pain (summarized in Table 23-2), underscoring that both peripheral and central mechanisms contribute to the pain and dysesthesias associated with central pain syndromes. Moreover, these data suggest that the targets of mechanism-based therapeutic interventions for central neuropathic pain may be found throughout the entire somatosensory system (from primary afferent to cerebral cortex), and a thorough understanding and evaluation of potential mechanisms is important for effective treatment.

ASSESSMENT

Physical therapy assessment of central neuropathic pain includes determining the neurological level of injury and gathering of information of pain-related factors [9,22,40,77]. The neurological level of injury is defined by the anatomical location of the injury, that is, brain, spinal cord, peripheral nervous system, or a combination of central or peripheral nervous system [9,40]. This may also include defining the (1) type of pain related to the diagnosis (e.g., musculoskeletal, nociceptive, or neuropathic), (2) pain-related factors (e.g., pain onset, description of pain, course of pain, pain symptoms, aggravating and relieving factors), (3) pain-specific measures (e.g., body diagrams quantitative sensory testing, McGill Pain Questionnaire, BPI, pain ratings, painDETECT), and (4) psychosocial screens (e.g., depression, anxiety, catastrophizing, fear) (Chapter 6). Disease-specific questionnaires and neuropathic pain questionnaires (NPQs) are recommended routinely in this population, although not all have been validated in all settings. These NPQs include Douleur Neuropathique 4 (DN4); Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) [14]; painDETECT [46]; NPQ [71]; and Neuropathic Pain Scale Inventory (NPSI) [19]. A systematic review by Mathieson et al. [78] found the DN4 and NPQ most suitable for clinical use.

TABLE 23-2 **Cellular Characteristics of Neuropathic Pain**

Central	Peripheral
Spontaneous ectopia (primary afferents, spinal cord, thalamus)	Spontaneous ectopia (primary afferents, spinal cord, thalamus)
Hyperexcitability	Peripheral sensitization
Neuroinflammation	Neuroinflammation
Structural plasticity (dorsal horn and DRG)	Structural plasticity (DRG)
Central sensitization	

Abbreviation: DRG, dorsal root ganglion.
Source: Adapted from Berger et al. [15] and Hulsebosch et al. [57], with permission.

MEDICAL MANAGEMENT

As with other chronic pain conditions, treatment of central pain syndromes is challenging. Important considerations in management of central pain syndromes are the comorbidities such as motor disturbances, cognitive dysfunction, and depression, which are frequently associated with many of the central pain disorders. Similar to peripheral neuropathic pain conditions, conventional

treatments for central neuropathic pain disorders include pharmacological, surgical, and interventional strategies.

Pharmacological approaches in the management of central neuropathic pain include antidepressants, anticonvulsants, opioids, and cannabinoids (as reviewed in reference [63]) (see Chapter 15). Based on systematic reviews, first-line pharmaceutical treatments for central neuropathic pain are tricyclic antidepressants (TCAs, antidepressants) and anticonvulsants (pregabalin and gabapentin) [4]. The high dose of TCAs may potentially cause side effects and pose safety concerns related to cardiovascular function. This may be a particular concern for patients with central pain because motor impairments, cardiovascular disease, and other conditions are common in patients with SCI, stroke, and neurodegenerative diseases. Antidepressants such as serotonin and norepinephrine reuptake inhibitors (SNRIs) are generally better tolerated than TCAs and have been suggested given their established efficacy in treatment for peripheral neuropathic pain conditions [63,108]. However, studies are limited and there is currently no support for the use of SNRIs in the management of central neuropathic syndromes associated with stroke, SCI, and MS [63,76]. Systematic reviews show that pregabalin and gabapentin are effective at treating central neuropathic pain in patients with SCI, stroke, and MS [63]. Strongest evidence for the use of another anticonvulsant drug, lamotrigine, has been established in central poststroke pain; however, studies with SCI and MS patients have failed to show effectiveness with these disorders [63,120].

Tramadol and other opioid analgesics are recommended as second- and third-line pharmaceutical treatments for central neuropathic pain [63,83]. As previously addressed in Chapter 15, there are risks of serious long-term side effects, as well as addiction and abuse associated with opioids. Other drugs, such as cannabinoids, have been shown as effective for central MS pain but failed to relieve neuropathic SCI pain [63].

Neurostimulation-Based Approaches

Noninvasive transcranial magnetic stimulation is a technique in which stimulation is applied over the cortex to produce an analgesic effect. Transcranial brain stimulation techniques have been investigated primarily in patients with SCI pain and include techniques such as transcranial direct current stimulation (tDCS), where current is applied over the sensory-motor cortex [32,86]. Evidence from randomized controlled trials (RCTs) indicates that tDCS is effective at reducing SCI pain in the short- and mid-term [18,80,105]. However, information on long-term analgesic effects have only been reported when

combined with visual illusion techniques, and safety issues using this treatment technique are lacking [63,86].

Spinal cord stimulation and epidural motor cortex stimulation (MCS) are invasive surgical techniques that are generally used for neuropathic pain that is refractory to standard medical treatments. Studies in patients with neuropathic SCI pain have shown that spinal cord stimulation may be most effective in treating at-level pain and those with incomplete spinal lesions [29,121]. Although studies are limited, emerging evidence suggests that MCS may be effective in treating central poststroke pain and facial pain [23,30]. Controlled trials are warranted for invasive neurostimulation-based approaches to demonstrate efficacy of this approach for refractory central pain conditions.

In summary, there is good evidence for the use of antidepressants, anticonvulsants, opioids, and cannabinoids for patients with specific central pain syndromes. However, significant side effects and safety of these drugs need to be carefully considered given the overlapping cardiac conditions and motor dysfunctions that might be impacted with use of these drugs. There is limited evidence to support the use of both noninvasive transcranial and spinal cord stimulator–based approaches, with efficacy for such approaches established mostly in the management of refractory neuropathic pain following SCI and stroke.

PSYCHOLOGICAL MANAGEMENT

Psychological management for chronic neurological pain has shown increasing strong evidence for hypnosis [35,61] and cognitive-behavioral therapy (CBT) for outcomes related to pain management, depression, anxiety, adjustment, and coping in SCI [37,80,81,89]. Evidence from a systematic review, meta-analysis, or RCT in psychological management specific to central neuropathic pain in traumatic brain injury is limited.

Systematic reviews have been done in MS with positive results for mind–body medicine [101] and modification of psychosocial factors [54]. RCTs have been done regarding education and psychological and peer support in MS [79] and efficacy of an Internet-delivered behavior intervention for symptoms and physical activity in MS [95].

Psychosis, apathy, depression, and anxiety are seen in PD. Management strategies for psychosis, apathy, depression, and anxiety include pharmacotherapy, behavior, and psychological approaches [47]. CBT in PD has

shown some initial benefits [36].

A literature review for patient education for nonpharmacological management in stroke [31] revealed challenges in methodology due to the multitude of symptoms addressed. An additional review demonstrated that stroke patients and caregivers reported needs about psychological changes in addition to patients' moving and lifting, exercise, and nutrition [51].

PHYSICAL THERAPY INTERVENTIONS

Overall there is paucity of evidence regarding effectiveness of physical therapy treatments for central neuropathic pain conditions. For most central neuropathic pain conditions, impaired mobility associated with motor disturbances is the central component of a patient's rehabilitation program. However, the development of pain syndromes strongly reduces quality of life. Patients with central neuropathic pain rate pain as one of the most difficult problems to manage, contributing to functional disability beyond those associated with mobility [119]. Given the impact on quality of life, it is critical that physical therapists address central neuropathic pain in an effort to maximize the patient's ability to participate in rehabilitation, facilitate return to functional activities, and improve overall quality of life (Table 23-3).

Transcutaneous Electrical Nerve Stimulation

Transcutaneous electrical nerve stimulation (TENS) is emerging as a safe and effective therapeutic approach for the treatment of pain in patients with specific CNS lesions [27,100]. Prospective, RCTs have shown that both low- and high-frequency TENS may effectively complement pharmacological treatment in patients with neuropathic SCI pain [26,90]. However, a recent Cochrane Review concluded a paucity of evidence to support the use of TENS in treatment of management of SCI pain [18]. A systematic review also showed conflicting evidence that TENS treatment reduces pain after SCI, supporting that TENS may be most effective at reducing at-level pain in patients with thoracic or cauda equine injuries, but not in those higher-level injuries [81].

TABLE 23-3 **Evidence for Physical Therapy Treatments of Central Neuropathic Pain**

Treatment	Type of Study	Results
TENS	Systematic review, RCT	Reduces pain (MS, SCI—at-level neuropathic pain)
Visual imagery	Double-blind trails	Reduces pain (SCI)
Exercise	RCT, case series	Reduces pain (SCI) and improves mobility (PD, MS)

Abbreviations: RCT, randomized controlled trail; MS, multiple scoliosis; SCI, spinal cord injury; PD, Parkinson disease; TENS, transcutaneous electrical nerve stimulation.

A systematic review examining the efficacy of TENS for management of central pain in MS showed Grade II (good) level evidence to support TENS as an effective pain management strategy in people with MS [100]. The use of electrical stimulation for the treatment of poststroke pain is limited, demonstrating that electrical stimulation may decrease glenohumeral subluxation resulting in reduced nociceptive shoulder pain [96]. Overall, these studies support that TENS may effectively complement pharmacologic treatments in patients with central neuropathic pain in MS and in specific subsets of patients post-SCI.

Visual Imagery

Newer treatment approaches include visual illusion, in which patients with SCI are placed in front of a screen aligned with an upper body mirror and lower body film projected to create an illusion of walking. Double-blind trails showed that neuropathic SCI pain was reduced for up to 12 weeks posttreatment [82,105]. A recent case report showed similar improvements in a patient with PD, showing that neurocognitive motor imagery training reduced lower limb pain [126].

Exercise

Similar to exercise-based approaches for peripheral neuropathic pain, exercise therapy for central pain is focused on improving and restoring function. In most central neuropathic pain conditions (PD, SCI, and stroke), exercise therapy exists as a part of management of overall health and management of the disease and associated impairments; however, the direct effect of exercise on neuropathic pain in these populations is unclear. In many instances exercise therapy effects on pain are rarely analyzed as outcome measures [50]; and when pain is assessed, it is often not clear if pain relief was neuropathic or musculoskeletal [24].

One study investigating the effects of a flexibility, relaxation, and walking program in people with PD reported improvement in pain with all forms of exercise [99]. Similar reductions in pain by exercise occur in those with neuropathic pain following SCI [91]. An intensive 10-week upper extremity poling ergometer exercise program (aerobic strength and conditioning activity) reduces both neuropathic and musculoskeletal pain following SCI [91]. A case series report also demonstrated similar reductions in neuropathic pain when patients with SCI were subjected to 60 minutes of overground bionic ambulation three times per week measured at light to very light intensity [72]. An RCT in patients with MS showed that both aerobic exercise and yoga reduced pain and improved mood and participation in functional activities [55]. Future studies are needed to evaluate effectiveness and dosing of exercise in those with central neuropathic conditions, but currently there is emerging evidence that exercise reduced pain in a variety of disorders of the CNS.

There is strong evidence from animal studies to support that exercise prevents or delays neurodegenerative processes associated with injury or disease of the CNS by restoring neuroplasticity, stimulating neurogenesis, and reducing immune responses, mechanisms that likely contribute to reducing and/or preventing central neuropathic pain [107] (see Chapter 10). Specifically, studies in SCI models show that exercise prevents aberrant sprouting of afferent fibers and the development of neuropathic pain following SCI [34,58].

In summary, evidence to support many interventions for the management of central neuropathic pain is limited. There is good support of TENS and limited support of visual imagery for treatment of central neuropathic pain conditions. Although evidence from controlled trials to support the use of exercise therapy for the treatment of central neuropathic pain is limited, exercise remains a cornerstone in the physical therapy rehabilitation of patients with SCI, stroke, PD, and MS. Exercise is also generally recommended for other peripheral neuropathic pain conditions, which share similar cellular characteristics to central pain syndromes (see Table 23-2). Based on this evidence, there is support for exercise as a component of comprehensive therapeutic strategies for managing patients with central neuropathic pain conditions.

As with other chronic pain conditions, treatment needs to be multimodal and multidisciplinary. Often, anxiety, depression, and psychological distress are significant secondary features of neurodegenerative disease, stroke, and SCI that need to be evaluated and treated. For most patients to achieve and maintain satisfactory pain relief, a combination of therapeutic approaches is necessary.

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CHAPTER 24

Case Studies

Kathleen A. Sluka and Carol G. T. Vance

The following 10 case studies describe pain in a selection of patients with a variety of diagnoses. Assessments are outlined, and normative values for tests are given where applicable. Under "Pain Assessment," the McGill Pain Questionnaire was used to obtain a sensory (S), affective (A), evaluative (E), and total (T) pain rating index (PRI). The VAS refers to pain intensity score on a visual analog scale. P1 and P2 refer to the first (onset) and second (maximal) point of pain in the range of motion (ROM) for the joint. A series of summary tables for different assessment measures are given so that the reader can directly compare patient responses across conditions. Table 24-1 shows a summary of answers to individual questions for the Pain Self-Efficacy Questionnaire (PSEQ) for individual cases, Table 24-2 shows a summary of SF-36 subdomains and the summary scores for individual cases, and Table 24-3 shows a summary of Patient Health Questionnaire scale (PHQ-2) and Generalized Anxiety Disorder scale (GAD-2) screening questionnaires for individual Cases 3–10.

Each case is followed by a general description of the rationale for the patient having peripheral, central, or neuropathic components to their pain and these are summarized in Table 24-4. We further address potential psychosocial concerns. The physical therapy treatment is then outlined, along with other treatments or referrals as appropriate. Finally, the clinical evidence to support the treatment plan is given, on the basis of the evidence presented in prior chapters. We send the reader to these chapters for further information.

These case studies are intended to serve as a tool for learning and synthesizing the evidence presented within this book. The reader should first review the cases and define the signs and symptoms that support different mechanisms underlying the pain and psychosocial concerns (we outline this rationale under "General Considerations"). The reader should then develop an evidence-based treatment plan on the basis of content presented in various chapters within the book. After developing the plan and reviewing the evidence,

reader should then read the treatment plan put forth by the authors and the evidence that supports this plan. We have placed the cases in two sections with the first section presenting the cases and assessment considerations and the second section presenting the general considerations and treatment for each case.

For each condition, the reader should always be aware of other disciplines that should receive a referral to help improve care. The ideal treatment of any patient with chronic pain is clearly multidisciplinary. If a multidisciplinary pain treatment facility is not available for the patient, then the therapist should strive to enable multidisciplinary care through active communication and interaction with healthcare providers in the community (see Chapter 11).

TABLE 24-1 Pain Self-Efficacy Questionnaire (PSEQ) for Cases

Question	Score					
	Case 1	Case 3	Case 4	Case 6	Case 8	Case 10
I can enjoy things despite the pain	6	3	3	5	1	6
I can do most of the household chores despite the pain	4	2	2	1	0	5
I can socialize with my friends or family members as often as I used to despite the pain	3	2	2	1	3	6
I can cope with my pain in most situations	4	3	4	0	3	5
I can do some form of work despite the pain	1	4	4	1	1	6
I can still do many of the things I enjoy doing such as hobbies or leisure activities despite the pain	1	3	4	0	2	3
I can cope with my pain without medication	3	4	3	2	0	6
I can still accomplish most of my goals in life despite the pain	6	5	6	2	2	6
I can live a normal lifestyle despite the pain	3	3	2	0	3	4
I can gradually become active, despite the pain	5	2	3	0	0	4
Total	36	31	33	12	15	51

Note: Answers from 0 to 6 with 0, not at all confident and 6, completely confident with a maximum total of 60.

TABLE 24-2 SF-36 Scores across Different Cases for Each Individual and Summary Scores

Domain	Case 1	Case 4	Case 5	Case 8	Case 9
Physical function	53	34	47	32	45
Role physical	35	28	42	35	35
Bodily pain	46	33	46	33	42
General health	58	41	60	37	51
Vitality	61	37	66	35	49
Social function	45	30	46	35	41
Role emotional	45	34	55	45	55
Mental health	60	39	62	44	57
Physical component summary	*44*	*30*	*42*	*28*	*35*
Mental component summary	*55*	*39*	*63*	*46*	*57*

Note: The scoring is norm-based with 50 as average. Scores below 50 are viewed as deficits in this area.

TABLE 24-3 PHQ-2 and GAD-2 Scores for Cases 3–10 for Questions 1 and 2 for Each Measure along with the Total

	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9	Case 10
PHQ								
1	3	2	0	3	0	3	1	1
2	3	2	1	3	0	2	1	0
Total	**6**	**4**	**1**	**6**	**0**	**5**	**2**	**1**
GAD								
1	2	3	1	0	1	2	2	0
2	3	1	0	0	0	2	1	0
Total	**5**	**4**	**1**	**0**	**1**	**4**	**3**	**0**

Note: PHQ-2 questions: Over the past 2 weeks, how often have you been bothered by any of the following problems? 1. Little interest or pleasure in doing things. 2. Feeling down, depressed, or hopeless. GAD-2 questions: Over the last 2 weeks, how often have you been bothered by the following problems? 1. Feeling nervous anxious or on edge and 2. Not being able to stop or control worrying. Answers: 0, not at all; 1, several days; 2, more than half the days; 3, nearly every day.

TABLE 24-4 Potential Underlying Mechanisms Associated with the Patients' Pain Including Peripheral, Central, Neuropathic, and Psychosocial Concerns

Case	Peripheral	Central	Neuropathic	Psychosocial
1	++	+	?	−
2	++	++	+	++
3	+	++	−	++
4	+	++	−	++
5	++	+	−	−
6	−	++	−	++
7	++	−	−	−
8	+	++	−	++
9	++	++	++	+
10	−	++	−	−

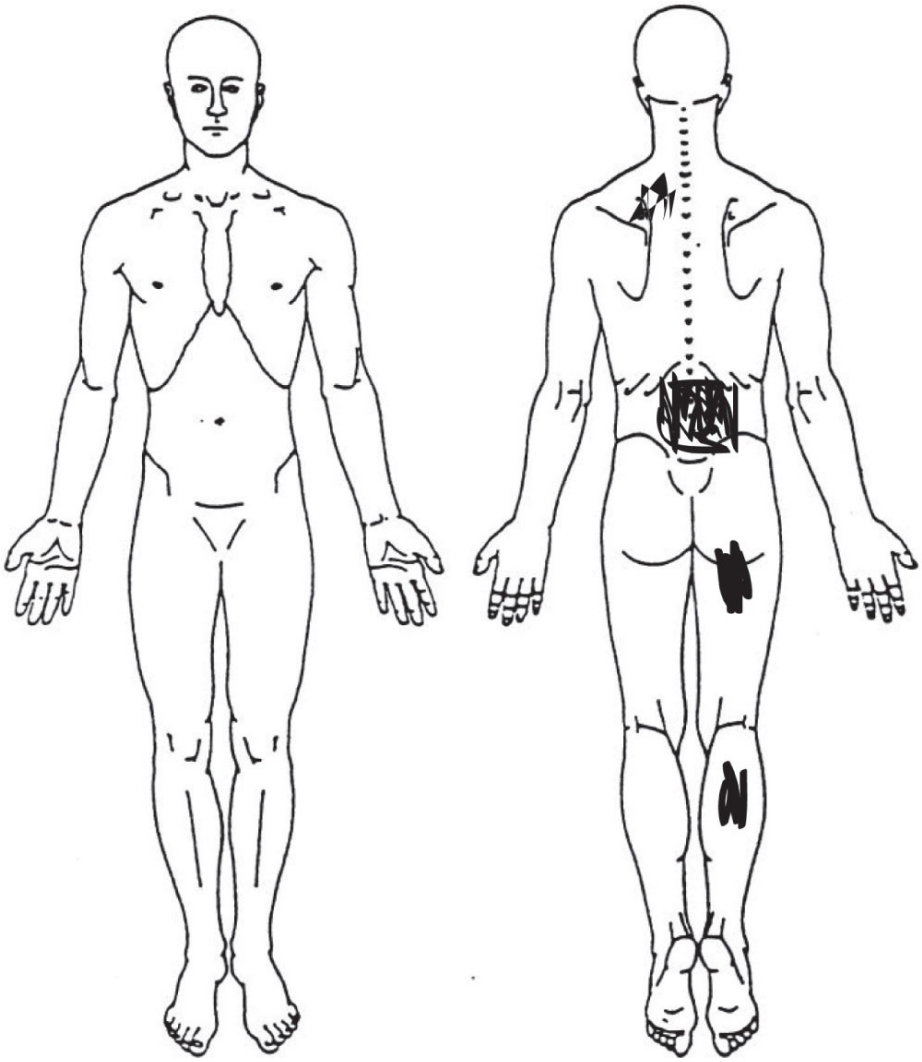
Abbreviations: +, minimal contribution; ++, strong contribution; −, no contribution.

SECTION 1: CASE PRESENTATION AND ASSESSMENT

Case 1

Subjective Assessment

This patient is a 42-year-old black male computer programmer who has a 4-month history of low back pain after having lifted a heavy suitcase out of his car. He states that the pain has not gone away as it did on other occasions when he had sprained his back. He decided to go to the doctor, who referred him to you for evaluation and treatment, stating that his X-ray showed some narrowing between some of the "back bones," and his magnetic resonance imaging (MRI) showed "bulging disks" in the lumbar spine. He reports that over the past few years he has had several bouts of low back pain that have lasted only a few days; otherwise, he is healthy and active and attends a fitness center three times per week. As the patient is talking, you observe that he is frequently rubbing his right calf, so you ask him if he has any other symptoms. He replies that his leg falls asleep a lot, but that "it is probably only poor circulation." He states that for the past 4 weeks or so, his right leg "sort of falls asleep and aches," and he feels it more when he sits down or bends over. When you ask what decreases it, he says the problem is always there but is not so bad on awakening and standing.



Pain Assessment

McGill Pain Questionnaire: Words chosen: cramping, tingling, dull, annoying. PRI-S: 6/42; PRI-A: 0/14; PRI-E: 1/17; PRI-T: 7/78. VAS score: 6/10 for lower back pain and 3/10 for leg symptoms. *P1 for lumbar flexion:* 10 degrees; *P2 for lumbar flexion*: 40 degrees.

Questionnaires

painDETECT: 15/38
STarT Back Screening Tool (SBST): 1/5
Roland-Morris Disability Questionnaire: 8/55
SF-36 (Table 24-2): Physical Component Summary (PCS): 44; Mental Component Summary (MCS): 55
PSEQ (Table 24-1): 35 with greatest concern for pain that interferes with

work, socialization, and hobbies

Objective Assessment

A gross *postural scan* shows that the patient's trunk has shifted to the left. He seems to be standing straight. There is guarding of the lumbar spine that creates a slight lumbar scoliosis to the left and a decreased lumbar lordosis. Trunk *active ROM*: flexion 40 degrees (limited by pain); extension 10 degrees (increases pain but is not limited by pain); side bending left 30 degrees; side bending right 10 degrees. Flexion and right side bending increase the patient's lower-extremity symptoms, so you ask him to remain standing in extension for a few seconds to see if it changes his numbness and pain. He says his leg feels better, but now his back is more uncomfortable.

As the patient tries to get into the supine position, you notice guarded transfers and grimacing, but once he is supine, he feels better. The patient then lies on his stomach and states that he cannot tolerate this position for very long because of back pain. You place a pillow under his abdomen for comfort and ask him how his leg and back feel now. Much to his surprise, the leg symptoms are considerably less (1/10), but his back continues to bother him.

Deep tendon reflexes for the lower extremity are normal. The patient reports diminished sensation to light tough on the posterolateral aspect of his right leg. His lower-extremity muscle *strength* is normal. *Straight leg raise test*, right: 30 degrees with increased low back and leg pain. Straight leg raise test, left: 70 degrees; pain free except for mild pulling on the hamstring muscles.

Assessment Considerations

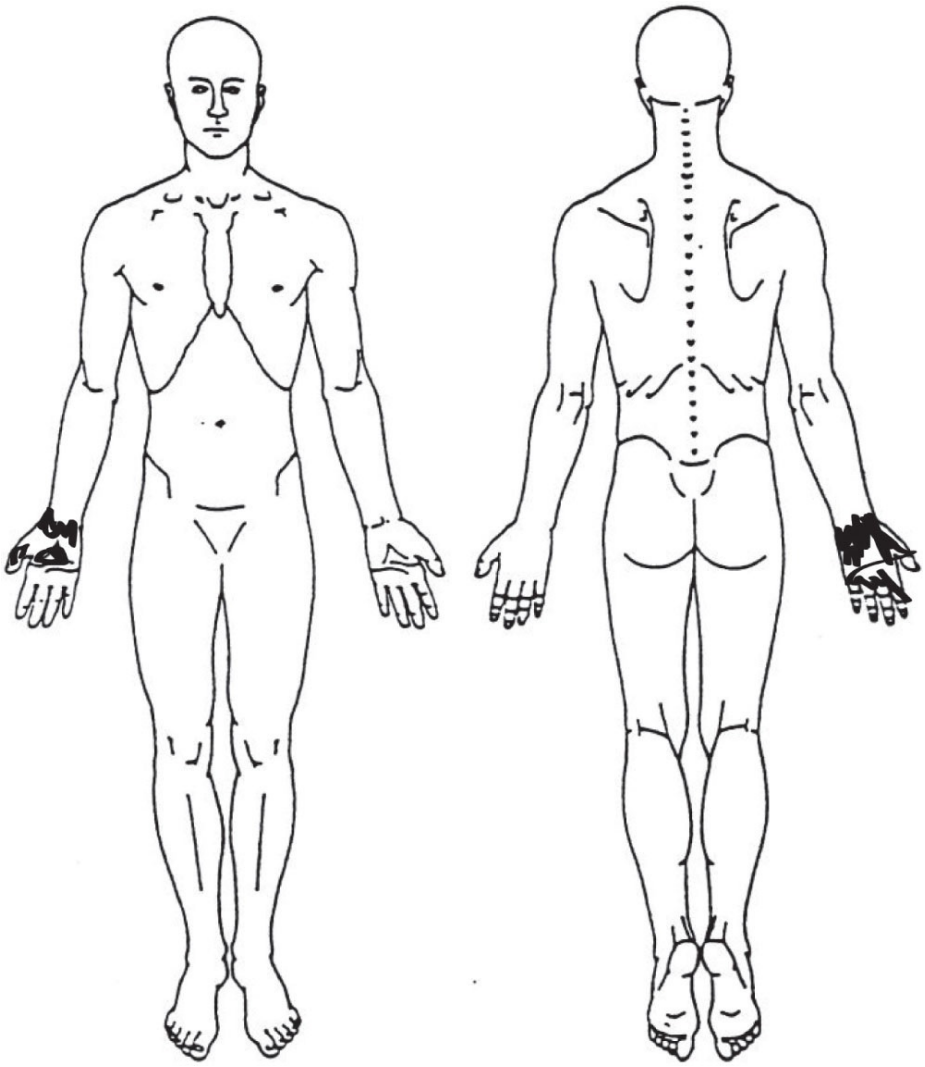
The McGill questionnaire was chosen because it is a multidimensional assessment of pain, includes a VAS pain rating, and offers the clinician a form of self-report of pain, which is considered the gold standard. In addition, the use of descriptive words may provide insight to the predominant cause of pain (neuropathic, vascular, musculoskeletal, or psychological). The painDETECT was chosen on the basis of patient history reporting diminished sensation to light touch and the results of the neurological examination (sensory, deep tendon reflex [DTR], and manual muscle test [MMT]). Because DTR and MMT were normal it is suspected that there is minimal nerve involvement, ensuring the patient belongs in the care of the physical therapist with a concurrent referral to the physician owing to the borderline painDETECT results. The nine-question SBAT was chosen because the injury is chronic and to screen for poor prognosis.

It can be useful in developing a plan of care to improve quality of life and efficient use of health care resources. The SF-36 only requires 5 minutes of the patient's time and is useful in detecting both positive and negative changes in health. The 10-question PSEQ was chosen to give the clinician information about the patient's perceived function specifically in relationship to their current pain condition. The Roland-Morris Disability Questionnaire was used on the basis of the results of the PSEQ indicating concerns related to work. This patient has a sedentary occupation potentially involving a great deal of time in sitting. Therefore, postural and ROM assessments will assist in guiding the exercise intervention. Patient education will be guided by all of the above assessments, particularly the PSEQ, Disability questionnaire, SF-36, and biomechanical assessments.

Case 2

Subjective Assessment

Mrs. H is an active 63-year-old, right-hand-dominant Hispanic woman who presents to you with a diagnosis of status post right Colles fracture sustained as a result of a fall in which she landed on her flexed wrist. She was immobilized in a cast for 6 weeks. The cast was removed 3 days ago. Mrs. H has limited understanding of English and her primary language is Spanish. She drives to her son's house daily to take care of her young grandchildren during working hours. She is widowed and lives independently but has a strong social support group from her church. Functional activity levels prior to the accident were normal. She complains of stiffness and pain, especially when she tries to move, and of inability to perform activities of daily living because she is so "right-handed." Her elbow and shoulder ache and feel stiff. She states that the cold outside makes the hand hurt much worse (the temperature outside is 20°F or −6.67°C), and she is unable to wear gloves because it increases her pain. As your examination commences, you realize that she is guarding her arm, which is maintained in a sling position even though there is no sling. Once she decides that she will let you evaluate the hand, you notice that the hand and wrist are swollen, paler, and cold to the touch compared with the left. The wrist appears somewhat malaligned. You are unable to test accessory joint mobility because of the patient's sensitivity to touch.



Pain Assessment

McGill Pain Questionnaire: Words chosen: pulsing, pricking, stinging, sore, fearful, troublesome, cold. PRI-S: 6/42; PRI-A: 1/14; PRI-E: 2/5; PRI-T: 10/78. VAS: 5/10.

Von Frey monofilament pain thresholds:

Index finger palmar distal interphalangeal joint (DIP)	Right 6 g	Left 180 g
Dorsal wrist	Right 26 g	Left 300 g

Questionnaires

WHOQOF-BREF: Physical 38, Psychological 56, Social 68, Environment 29
TSK: 56

PCS: 36
painDETECT: 8/38

Objective Assessment

Active ROM: wrist extension: 10 degrees; wrist flexion: 5 degrees; ulnar deviation: 5 degrees; radial deviation: 5 degrees; supination: unable to obtain neutral; pronation: 30–60 degrees; elbow: 20 to 100 degrees.
Strength: wrist extension: 3/5, within available ROM; wrist flexion: not tested; grip dynamometer: right 3 pounds (1.4 kg), left 40 pounds (18 kg).

Assessment Considerations

Traditional ROM, MMT, and grip strength assessments in conjunction with pain measures guide the clinician's choice of dynamic exercise and functional training interventions. The Von Frey filament testing was done to assess for allodynia on the basis of her statement that putting on a glove caused increased pain. In addition, the painDETECT was used to determine any potential neuropathic component on the basis of her subjective complaints. The World Health Organization Quality of Life Survey (WHOQOL)-BREF was chosen to measure quality of life in this Spanish-speaking individual. The use of the McGill questionnaire includes a VAS pain rating and offers the clinician a form of self-report of pain, which is considered the gold standard. In addition, the use of descriptive word "fear," as well as the presentation of arm guarding, prompt the clinician to consider assessment of fear of movement and reinjury using the TSK, and the 13-question PCS can be used to assess the potential involvement of magnification, rumination, and helplessness on the basis of her WHOQOL-BREF score. The TSK and PCS are also available in Spanish.

Case 3

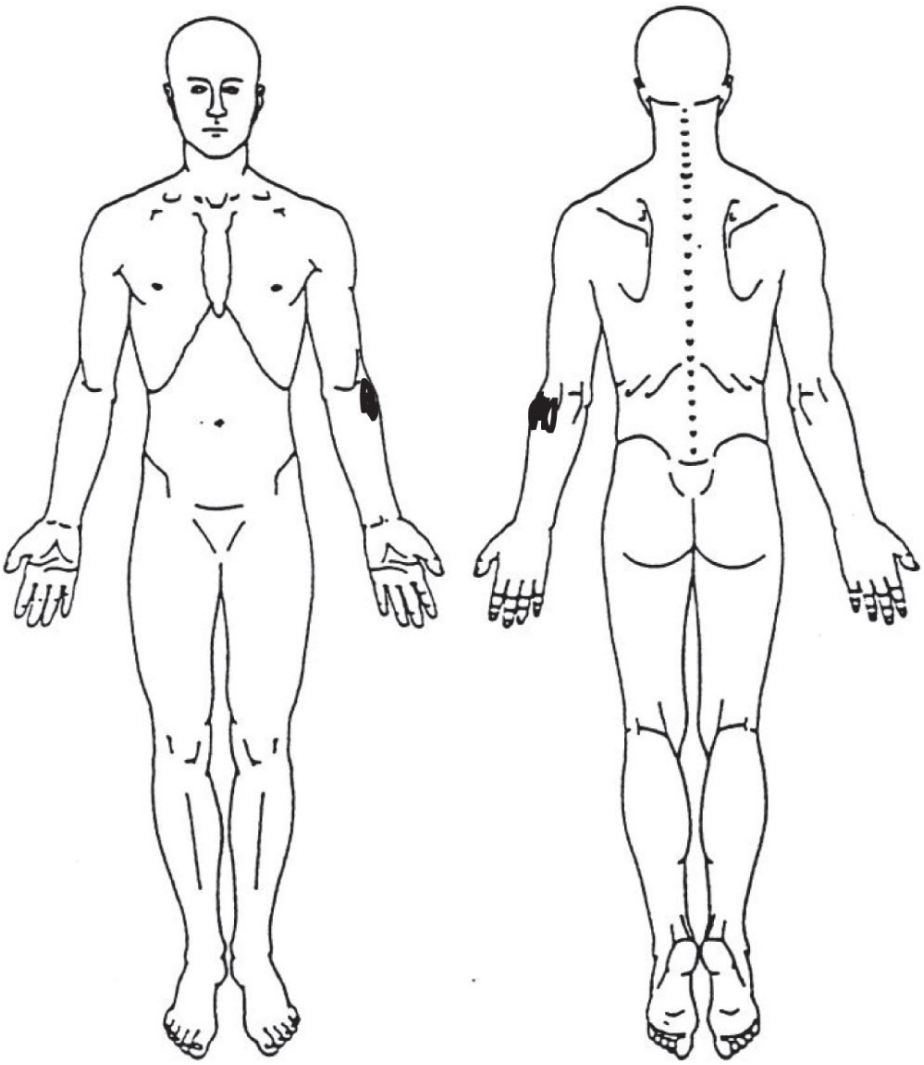
Subjective Assessment

This patient is a 35-year-old, left-hand-dominant male dentist with complaints of left elbow pain of 1-year duration that has gradually worsened. He states that there is no specific injury, but he notices the pain more after working a full day and after playing racquetball. However, the patient is not experiencing discomfort at rest. He decided to prescribe anti-inflammatory drugs for himself,

but they have given him only mild relief. He saw an orthopedic surgeon, who injected the painful area with an anesthetic and a corticosteroid, but he continued to feel pain when performing work and sports. He has already been to see a physical therapist, who gave him ultrasound, ice, stretching exercises for the wrist, and an arm band.

The patient feels more pain as the day progresses. He wakes up at night only if he sleeps on his arm; in the morning he wakes up feeling relatively well, albeit somewhat stiff. He rates his pain during activities as 6/10 (verbal rating scale), describing it as a “toothache in his arm.” He states that he has not experienced any numbness or tingling, but that his pain does occasionally radiate down into his knuckles, and he now fears that his work and patients may be at risk if this symptom continues. He demonstrates to you that merely upon extending his wrist he feels pain. The patient has no history of heart disease, diabetes, psychological illnesses, cancer, or arthritis. He reports no previous injury of the arm and reports his general health status as excellent. He is the sole breadwinner and has a supportive spouse and family. He states that he has a good life that would be “great” if he could get rid of his arm pain.

Case 3



Pain Assessment

VAS at rest: 1/10; VAS with grip: 5/10

Questionnaires
PHQ-2 (Table 24-3): 6/6
GAD-2 (Table 24-3): 5/6
PSEQ (Table 24-1): 31 with significant problems in all domains
BPI: Severity (Intensity) 3; Interference 6
Quick DASH: 5.74 (mean norm for males 35–44 = 6.72)
TSK: 38
PCS: 9
CPSS: PSE 150/500, PFE 550/900, CSE 380/800

Objective Assessment

Girth measurements taken with a tape measure reveal no difference between right and left sides. *Palpation* of the extensor muscle group reveals a positive twitch response with increased localized pain. Light palpation of the head of the radius, the radiohumeral joint line, and the lateral epicondyle increases pain. A general inspection shows that the proximal posterior forearm is warmer to the touch than the noninvolved side, and the tissue feels edematous ("boggy") in the same area. Testing of *accessory joint motion* shows that radiohumeral and ulnohumeral joint distraction and radiohumeral anterior–posterior glides are not restricted but are positive for pain at Grade III.

Active ROM: wrist flexion: 75 degrees; wrist extension: 50 degrees; pronation: within normal limits; supination: 80 degrees. Passive ROM: wrist flexion: 85 degrees; wrist extension: 65 degrees; pronation: within normal limits; supination: 80 degrees. Finger, elbow, shoulder, and cervical ROM: WNLs.

Strength: wrist extension: 4/5 with pain; wrist flexion: within normal limits. Grip dynamometer: left 65 pounds (29 kg), right 100 pounds (45 kg).

Assessment Considerations

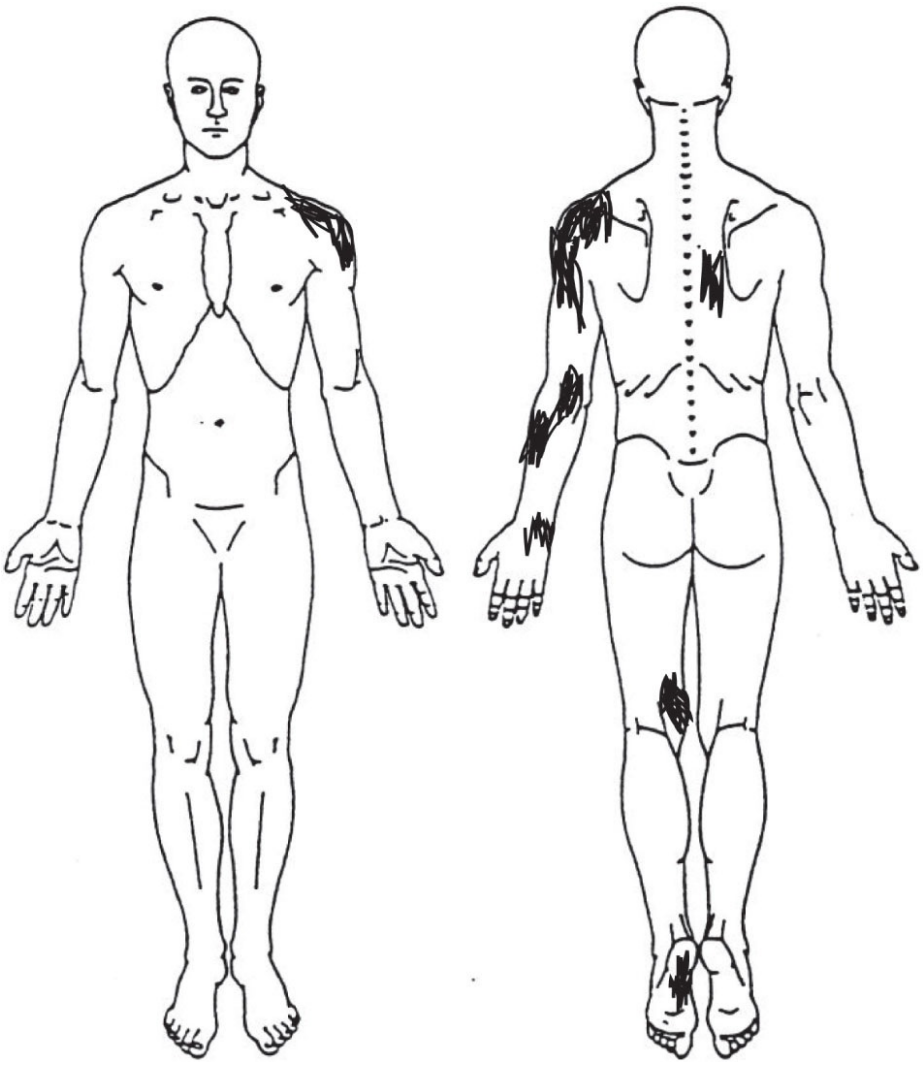
Traditional measures of inspection, palpation, ROM, MMT, girth measurement, palpation, accessory joint motion, and grip strength provide the baseline information to the therapist when constructing the intervention plan. As depression and anxiety are highly correlated with chronic pain, we performed the 2-question screening tools, PHQ-2 and GAD-2, and both scores indicate additional assessment is warranted by the physician or psychologist. Using the VAS at rest and with movement allows the clinician to determine if interventions directed at pain with movement will be important. In this case, movement pain is uniquely different than resting pain (see Chapter 2), and, of note, movement pain does not respond to traditional opioid analgesics. With the patient's expression of concern for his patients and his ability to pursue his role as a dentist the Quick DASH and BPI were utilized to assess the impact of pain on function. Because of the chronicity of the condition the CPSS was used to assess ability to cope in relationship to general activity, mood, work, relationships, sleep, and enjoyment of life, and TSK and PCS were used to assess for other potential psychological confounders. The results of these psychosocial assessments support the results of the depression and anxiety screening questions.

Case 4

Subjective Assessment

This patient is a 50-year-old, left-hand-dominant, Asian female who presents with gradual onset of left shoulder pain that started approximately 6 months ago without apparent cause. She complains of a constant dull ache that radiates from her shoulder to the dorsal aspect of the forearm. The ache increases with motion and decreases with rest. She comes to you now because of increased difficulty reaching overhead and combing her hair. She works as a clerk and lately has needed help to retrieve file boxes located on top of the filing cabinets. She relates no prior history of left shoulder problems but states that she had bursitis of the right shoulder 10 years ago, which resolved with cortisone injections. Thinking that she had the same thing on the left side, she asked her doctor if he could inject it. Two shots over the last 3 months did not diminish her symptoms, nor has she attained significant relief with nonsteroidal anti-inflammatory drugs (NSAIDs). She reports she is becoming very discouraged and no longer even wishes to participate in things that in the past were important to her (shopping with friends, attending church service or related activities, and gardening). Other medical history includes a hysterectomy 7 years ago and hypertension that is controlled with medication. She also takes calcium supplements at her physician’s request. Otherwise, she is healthy and sedentary.

Case 4



Pain Assessment

McGill Pain Questionnaire: Words chosen: throbbing, gnawing, aching, fearful, miserable, nagging. PRI-S: 11/42; PRI-A: 3/14; PRI-E: 3/5; PRI-T: 18/78. VAS: resting 7/10; with arm elevation 9/10. Patient has significant guarding of the shoulder. P1 for external rotation of the shoulder = 5 degrees; P2 for external rotation of the shoulder = 25 degrees.

Questionnaires
PHQ-2 (Table 24-3): 4/6
GAD-2 (Table 24-3): 4/6
Quick DASH: 6.01 (mean norm for females 45–54 = 13.01)
FABQ: Physical activity 22/24, Work 24/48
TSK: 29

SF-36 (Table 24-2): PCS 30; MCS 39
PSEQ (Table 24-1): 33 with greatest concern for pain that interferes with living a normal life and getting along without pain medication

Objective Assessment

The patient's *posture* shows a mild kyphosis—rounded shoulders and a forward head. Scapular position reveals the medial angle of the left scapula to be one-half inch (approximately 1.3 cm) higher than the right. Scapulothoracic rhythm is asynchronous.

ROM: Cervical ROM is complete, but with a feeling of tightness on the left during right-side bending. Right shoulder ROM and strength are within normal limits. Left shoulder: active ROM: flexion: 96 degrees; extension: 30 degrees; abduction: 63 degrees; adduction: within normal limits; external rotation: 25 degrees; internal rotation: 70 degrees. Passive ROM: flexion: 115 degrees; extension: 35 degrees; abduction: 110 degrees; adduction: within normal limits; external rotation: 30 degrees; internal rotation: 50 degrees.

Accessory *joint motion* of the left glenohumeral joint: hypomobility in anterior and inferior directions.

Manual muscle testing: 3+/5 on all shoulder girdle muscles, with the exception of external rotation, which is 3/5. All manual muscle test values are done within the available range.

Palpation of shoulder region: diffuse tenderness of the upper trapezius, the medial border of the scapula, and the anterior and lateral shoulder.

Assessment Considerations

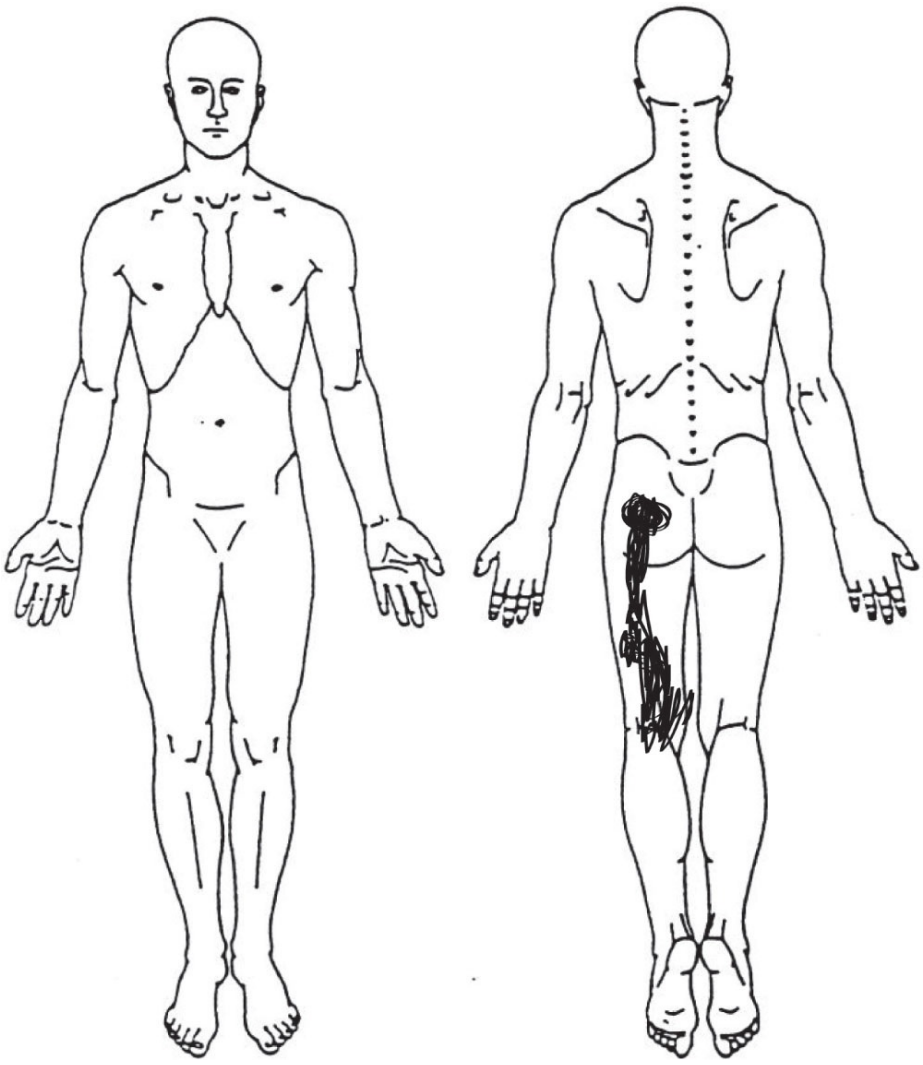
Cervical and glenohumeral ROM, postural and scapular thoracic rhythm assessments, MMT, accessory motion, and palpation provide the foundation for clinical decision making as the therapist organizes the dynamic interventions of exercise and functional training in this case. The MPQ was chosen to obtain the affective dimension of pain by words chosen as well as obtaining self-reported pain intensity. The words chosen "throbbing, gnawing, aching, fearful, miserable, nagging" along with the subjective information of loss of interest in activities provide clear indication to pursue screening for depression, anxiety, and fear of movement. The FABQ was used because of the chronicity of the condition and guarded posturing, and has been utilized in patients with shoulder conditions. In addition, the TSK was used to screen for potential problems with

her acceptance of a dynamic portion of the treatment intervention. Because there are significant impairments in strength and ROM, the SF-36, self-efficacy, and DASH scores are employed to assess disability and function in relation to the pain condition.

Case 5

Subjective Assessment

This patient is a 44-year-old black woman who states that she developed left lower-extremity pain about 3 months ago. She has no history of trauma or inappropriate lifting. Pain increases to a 10/10 at times, and it is felt all the way down to the foot, especially with prolonged sitting. The medical history is unremarkable. Examination reveals a slightly overweight female. Posture is normal, with the exception of a slight bilateral genu recurvatum and outward toe position (45 degrees). Her trunk ROM is normal without reproduction or relief of pain, except for a tight feeling in the left posterior thigh during forward flexion. She works as an engineer, spending most of her time sitting and working at a computer. She does not exercise on a regular basis.



Pain Assessment

McGill Pain Questionnaire: Words chosen: shooting, crushing, intense, radiating, agonizing. PRI-S: 8/42; PRI-A: 0/14; PRI-E: 4/5; PRI-T: 15/78. VAS at rest: 4/10.

Questionnaires
PHQ-2 (Table 24-3): 1/6
GAD-2 (Table 24-3): 1/6
SF 36 (Table 24-2): PCS 42; MCS 63
painDETECT: 6
SBST: 2/9
Oswestry (ODI): 26.6

Objective Assessment

Special tests: Left straight-leg raise is positive for left leg pain at 60 degrees; deep tendon reflexes and sensation to light touch are intact; Slump test and Gillet test are negative.

Manual muscle tests: 4+/5 for the left lower-extremity muscles, except for external hip rotation, which is 4/5 with slight pain; 5/5 for the right lower-extremity muscles, except for external hip rotation, which is 4/5.

Palpation: tenderness on the left sacroiliac joint area and the left mid-buttock toward the greater trochanter. Pain in the leg is reproduced with pressure over the mid-buttock. With the hip in 90 degrees flexion, stretching into hip internal rotation is painful during the stretch but results in slightly reduced pain after the stretching is finished.

Active Hip ROM: flexion: right 120 degrees, left 110 degrees; extension: right 15 degrees, left 15 degrees; abduction: right 45 degrees, left 40 degrees; adduction: right 40 degrees, left 40 degrees; internal rotation: right 35 degrees, left 20 degrees; external rotation: right 45 degrees, left 45 degrees.

Functional Tests

Resting heart rate (HR) 68, BP 128/80
6MWT 171 m, HR 104, BP 132/82, Pain NRS 6
Five times sit to stand (5TSTS) 5.3 seconds, HR 88, BP 130/84, Pain NRS 5

Assessment Considerations

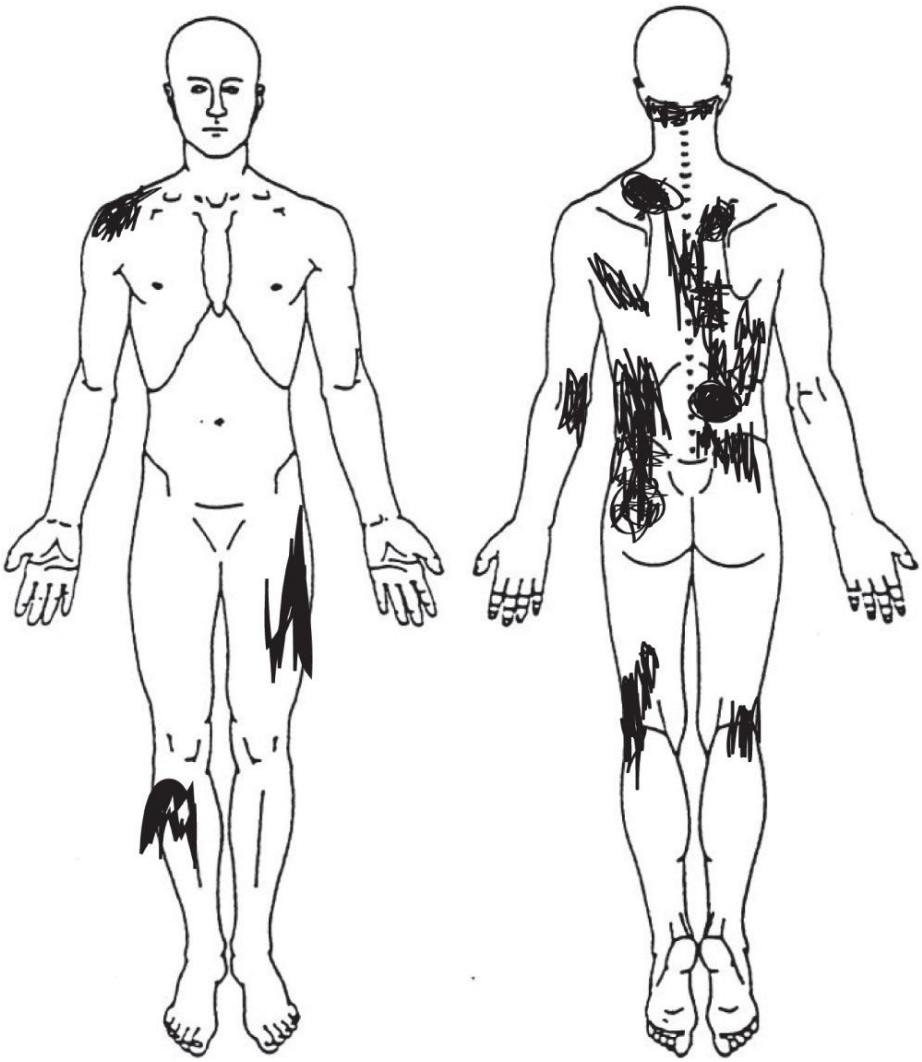
The painDETECT to screen for neuropathic pain and SBST to screen for risk of poor prognosis for treatment were indicated by the patient's comments of 10/10 pain with no apparent injury and results of the battery of traditional objective assessments (ROM, MMT, palpation, neurologic screen, posture, and special tests). SF-36 was the tool chosen to assess the association of pain and function in this patient. In addition, the disease-specific Oswestry screen was used to yield more useful results specifically for LBP. The Roland-Morris screen would also be a reasonable choice. The screening questions for anxiety and depression are used in all patients to determine if additional screening and referral will be indicated. The 6MWT and 5TSTS tests along with NRS pain assessment during movement provide functional measurements and the impact of pain on function. The patient's performance on these tests was below the norms in comparison with age-matched females, and she was able to achieve 60% of age-predicted

maximal heart rate. The functional tests were chosen because of the patient's sedentary job and lifestyle to assess baseline physical functioning to assist in developing an exercise prescription and monitor improvement over time.

Case 6

Subjective Assessment

This patient is a 45-year-old white woman who came into the office complaining of pain that has gradually worsened over the last year. It initially started in her shoulders, extending down her arms and into her hands. The pain also seems to travel up into her neck and cause "migraine" headaches. Later on, she felt pain in her lower back, her legs, and her feet. She now feels as if her whole body is in a state of constant pain. The pain came on gradually, without any preexisting traumatic episode. She also complains of difficulty sleeping and says she has not slept an entire night in the last 6 months. She lives alone in a ranch-style home with a ½-acre yard and is distressed about not being able to keep up with home and yard duties. She is unable to work, garden, or do her normal walking because she is too tired. She complains of not having enough energy to even do the housework regularly. She says she has gained 30 pounds (13.6 kg) in the last year because she has been unable to do anything physical. She says she used to be a very active person and now cannot do anything because of the pain.



Pain Assessment

McGill Pain Questionnaire: Words chosen: pounding, stabbing, crushing, wrenching, heavy, splitting, exhausting, suffocating, terrifying, vicious, wretched, unbearable, spreading, tight, dreadful. PRI-S: 27/42; PRI-A: 12/14; PRI-E: 5/5; PRI-T: 68/78. VAS: sensory-discriminative scale: 6/10; motivational-affective scale: 8/10.

Questionnaires

PHQ-2 (Table 24-3): 6/6

GAD-2 (Table 24-3): 0/6

PSEQ (Table 24-1): 12 with significant problems in all domains, including inability to enjoy social activities, perform household chores, go to work, and cope with the pain

TSK: 29
PCS: 40
BPI: Severity (Intensity) 7.5; Interference 9.3
FIQR: 77
Sleep follow-up questions:
Do you have trouble falling asleep? No
Do you have trouble staying asleep? Yes
How many times do you wake up during a typical night? Seven to eight times
Do you wake up refreshed? No

Objective Assessment

Height: 66 inches (1.676 m); Weight: 240 pounds (109 kg); body mass index (BMI): 38.7; RHR: 78; RBP: 128/84; RRR: 13.

Postural scan: rounded forward shoulders, forward head, increased lumbar lordosis, and protuberant abdomen. Genu valgum, slight knee hyperextension, and pes planus.

Palpation: Multiple tender points located bilaterally at the occiput, C5–C7, trapezius, second rib, lateral epicondyle, gluteal region, and left medial knee.

Strength, trunk manual muscle testing: lower abdominals: 1/5; upper abdominals: 2/5; thoracic/lumbar extension: 3/5.

Functional assessments, 6-minute walk test: 91.44 m but the patient stops after 3 minutes and refuses to complete the test because of increased pain and distress. NRS pain intensity 10. NRS fatigue 9. Post walk vital signs: HR 144, BP 144/88, RR 22.

Assessment Considerations

The subjective history provided by the patient talking about widespread pain, fatigue, sleep disturbances, body diagram, and self-efficacy screen offers clues to direct further assessment. Posture, palpation, and ROM assessments are quickly followed with the BPI for pain interference (sleep, work, mood, relationships, joy in life) and FIQR as a disease-specific tool that should be offered to the patient with a suspected diagnosis of fibromyalgia. These assessments are favored over numerous special tests for LBP, neck pain, and accessory joint mobility available to the therapist. The TSK and PCS are indicated by the patient's report of fear of not being able to keep up with her life activities and

her use of the word “exhausting and terrifying” in the MPQ. NRS for pain intensity and fatigue at the point of peak exercise in the 6MWT as well as rest and exercise vital sign values will assist in developing a safe and effective aerobic conditioning program. The follow-up sleep questions are indicated by the patient’s subjective report that she has not had a good night sleep in many months. In this case, the screening for anxiety and depression, self-efficacy, and 6MWT are the tools that will have most impact in developing the intervention strategies and uncovering potential concerns requiring a multidisciplinary approach.

Case 7

Subjective Assessment

This patient is a 31-year-old white man who was playing basketball 2 weeks ago and “twisted” his right ankle, resulting in a Grade II sprain. He did not see a physician until 3 days ago. The physician put him in a removable ankle brace and sent him to physical therapy. He drives and delivers for a local beer distributor. He says he has difficulty driving and finds it difficult to unload the truck. He is currently on sick leave. He has no significant medical history.

Pain Assessment

The patient complains of pain around the ankle that sometimes radiates into the calf and lower leg. Pain is rated at 4/10 at rest and at 8/10 when standing. There is increased pain with pressure on the lateral portion of the ankle (the anterior talofibular ligament and surrounding soft tissue).

Questionnaires
PHQ-2 (Table 24-3): Total 0/6
GAD-2 (Table 24-3): Total 1/6
SBST: 1

Objective Assessment

Patient ambulates with an antalgic gait with decreased stance time on the right. Observation during ambulation also reveals obvious pain behaviors of grimacing and auditory wincing during stance on the right. He has obvious swelling around the ankle joint and decreased active ROM (50% or greater decrease in plantar

flexion, dorsiflexion, and internal and external rotation of the ankle). All ROMs are limited as a result of pain. Passive ROM is similar and has an empty end feel (absence of end feel when patient stops movement before sensing resistance). Isometric break test indicates patient is able to meet resistance for all ankle motions with 8/10 pain during resisted ankle eversion.

Assessment Considerations

The 2-question screens for depression and anxiety are negative in this case and thus there is little concern of psychological factors that need to be addressed in this patient. Because the patient delayed seeking care for his injury for 10 days, the SBST was used to provide a quick assessment of risk of poor prognosis, and again shows no concerns agreeing with our depression and anxiety screens. Given the time frame from injury (i.e., acute pain condition), assessments of gait, ROM, strength, end-feel, observation, and palpation, in conjunction with pain ratings and the psychological assessments outlined above, provide sufficient information to design the initial plan of care to treat this patient. The physical therapist should confirm that radiographs were ordered and evaluated by the physician prior to initiation of treatment.

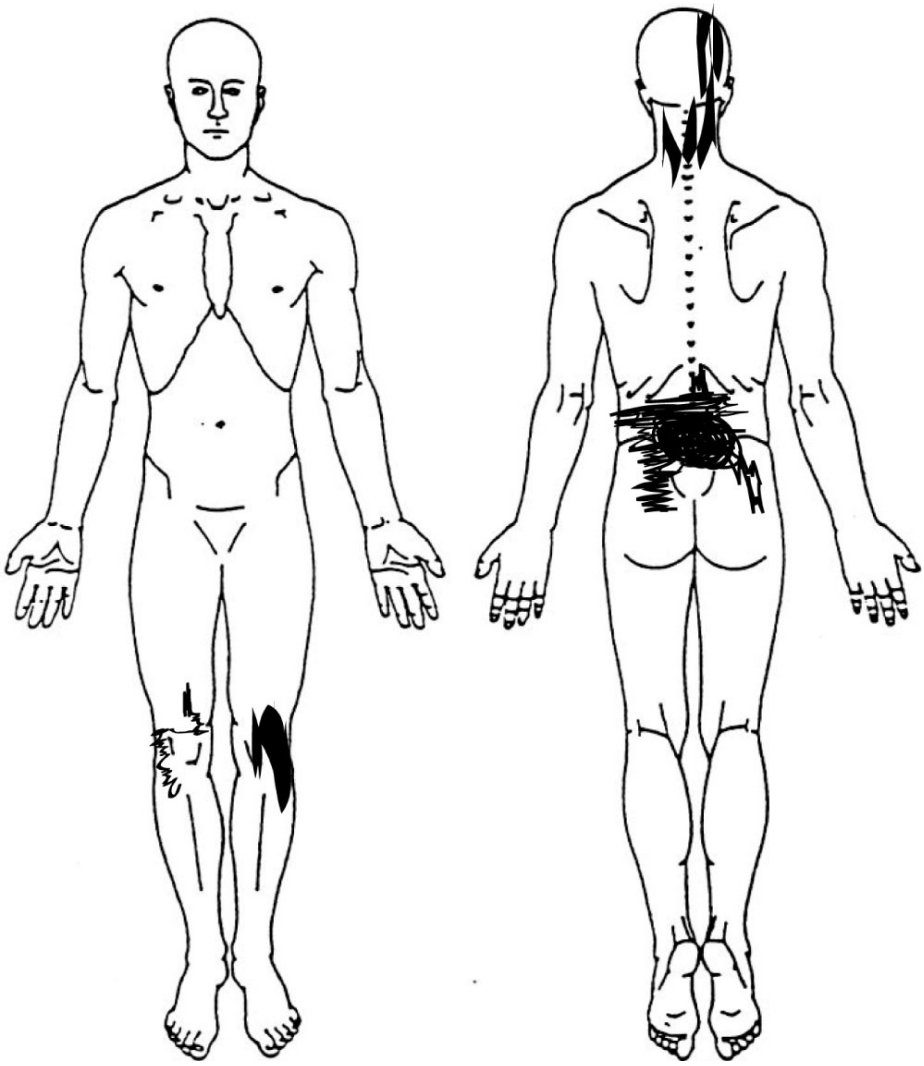
Case 8

Subjective Assessment

This patient is a 45-year-old white woman who complains of low back pain that started 10 years ago after an automobile accident. The pain is in the lower back, the left hip, and the back of the left thigh. The pain is worse with walking and better with sitting. However, if the patient sits too long, the pain again increases. She can sit for about 2 hours before she has to get up because of the pain. She says she is also tired all the time and is sore in the upper back and both legs. She reports pain and tenderness in the upper back and legs. She has difficulty concentrating during the day and does not sleep well and never awakens refreshed. She was initially able to work for the first year after the accident, but the pain has become progressively worse, and now she cannot work. She works as a secretary for a university department of anthropology and has been on an extended leave of absence for the last 3 months. She had X-rays, an MRI scan, and nerve conduction tests 3 years ago, all of which are normal. The MRI done last week showed degenerative changes at the L2-3, L3-4, and L4-5 with bulging

discs at L3-4 and L4-5. The patient states she now has a reason for her pain. She does not routinely exercise and did not do so before the accident (she says she did not have the time to do so, although she knows it is important). Previous treatments include exercises given by her family practitioner and medications consisting of muscle relaxants, naproxen, and acetaminophen (paracetamol) with codeine. She is now attending the multidisciplinary pain clinic at the university.

Case 8



Pain Assessment

McGill Pain Questionnaire: Words chosen: pounding, shooting, stabbing, cramping, cramping, tingling, aching, exhausting, frightful, cruel, intense, radiating, agonizing. PRI-S: 22/42; PRI-A: 7/14; PRI-E 4/5; PRI-T: 38/78. VAS

for pain in the lower back: 5/10; for pain in the hip: 4/10; for pain in the leg: 2/10.

Questionnaires
PHQ-2 (Table 24-3): 5
GAD-2 (Table 24-3): 4
SF-36 (Table 24-2): PCS 28; MCS 46
PSEQ (Table 24-1): 15 with the most significant problems in work capability and hobbies
BPI: Severity (Intensity) 4.25; Interference 7.4
FABQ: Physical activity 23; Work 49
PCS: 17 (Rumination 5, Magnification 2, Helplessness 10)
Roland-Morris: 17

Objective Assessment

Vital signs: HR 88, BP 136/80, RR 12.
Posture: forward head, forward shoulders, flattened lumbar lordosis.
Strength: upper abdominals 3/5; lower abdominals 2/5; back extensors 2/5; hip extensors 3/5. Straight-leg raise, left: positive for pain in the low back at 45 degrees; hamstrings are tight. Straight-leg raise, right: positive for pain in the low back and leg at 60 degrees; hamstrings are tight.
Palpation: tenderness over the lower back bilaterally with greater tenderness on the left side. The patient has mild muscle tightness over the left back. She also has tenderness over the hip area, and it hurts to shift her body weight and sit on the left hip.
Lumbar active *ROM* is reduced: forward flexion: 50%: extension: 0%, with pain; side bending, right: 20%; side bending, left: 50%, with pain; rotation, right: 10%; rotation, left: 10%. Hip ROM is reduced: flexion: 100 degrees; pain in back; internal rotation: 30 degrees, with pain; external rotation: 30 degrees, with pain; extension: 0 degrees (unable to do).
Function tests: 5TSTS 5.9 seconds with NRS pain 7, NRS fatigue 7. 6MWT 522 m with NRS pain 8, NRS fatigue 9, HR 126, BP 168/90, RR 20.

Assessment Considerations

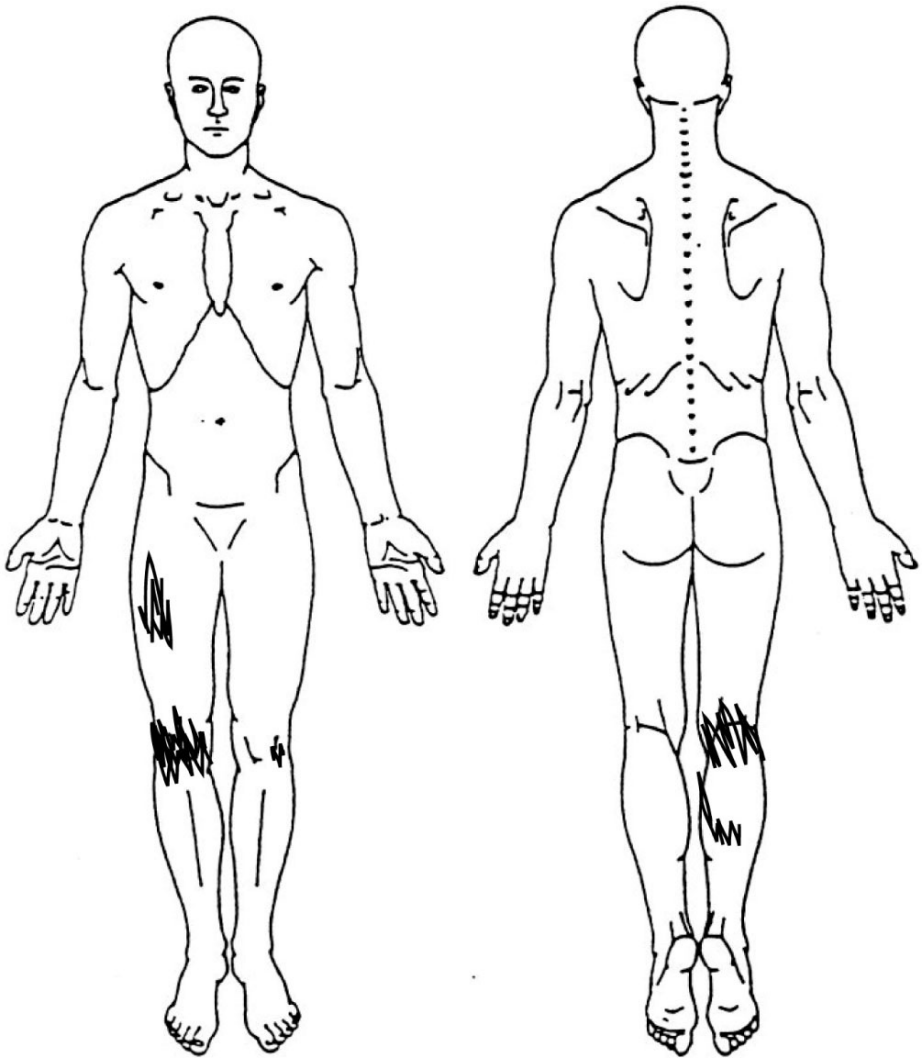
For this case it is important to note the findings of prior assessments (radiographs, MRI, nerve conduction velocity/electromyography [NCV/EMG]) so as to include them in your discussion with the patient as pertains to the

therapist examination and treatment. Standard impairment assessments of ROM, strength, posture, palpation, and SLR testing as well as vital sign measurement are required elements necessary to make determinations of appropriate dynamic interventions. HR and BP response to exercise will be used to develop and appropriate aerobic component of the plan. A battery of additional special test to examine for spine pathology and biomechanics is not indicated to develop a treatment plan in this patient (i.e., 10 years since original injury). The potential exists to further disappoint the patient in her search for "the cause," and could be a barrier to successful participation in the active management of her chronic pain condition. The MPQ, self-efficacy, and SF-36 have appeared consistently in previous cases and their use is important here as well for reasons previously stated. The additional questionnaires (TSK, FABQ, PCS, BPI, and Roland-Morris) could be administered over several treatment sessions so as to decrease patient burden. These assessments were used on the basis of the results of the screens for depression and anxiety, results of the SF-36 and self-efficacy questionnaires, and the decline in work status over time. The TUG test could replace the 6MWT to decrease patient burden if indicated; however, the changes noted in vital signs would most likely not be appreciated in this significantly shorter walking test.

Case 9

Subjective Assessment

This patient is a 54-year-old married white woman with a part-time job as a greeter at a discount department store. She has been diagnosed with Grade II osteoarthritis of the right knee joint by a rheumatologist, with the initial diagnosis 4 years ago. She is currently taking tramadol, acetaminophen (paracetamol), and aspirin for the knee pain. Her height is 5 feet 6 inches (1.71 m), and her weight is 249 pounds (113.2 kg) (BMI = 40). She has high blood pressure and diabetes that are controlled with medications. Otherwise, she says she is generally healthy. Her pain is better when she wakes up in the morning, but it gets worse as the day progresses. She becomes restless at work and is becoming anxious about her potential to continue in a job that she enjoys.



Pain Assessment

Her current VAS pain rating at rest is 2/10, but she says it is as high as 7/10 when climbing stairs, which is a problem for her because she lives in a two-story house with a basement and has to climb stairs daily to do laundry and get to the bedroom.

Questionnaires

PHQ-2 (Table 24-3): 2
GAD-2 (Table 24-3): 3
The WOMAC shows a function score of 1465 (range 0–1700), a pain score of 393 (0–500), and a stiffness score of 155 (0–200)
SF-36 (Table 24-2): PCS 35; MCS 57
painDETECT: 20

Objective Assessment

Palpation of the knee reveals tenderness to pressure along the medial joint line of the right knee. *Pressure pain thresholds* of the knee (medial joint line): right: 145 kPa/s; left: 279 kPa/s; over the tibialis anterior: right 165 kPa/s, left 349 kPa/s.

Active ROM of the right knee is 0 degrees extension and 110 degrees flexion and is limited by soft-tissue approximation. Her left knee joint has the same ROM.

The *strength* of the right knee is 3+/5 for knee extension and 4/5 for knee flexion. The strength of the left knee is 5/5 for both extension and flexion.

Functional tests: Timed up and go test: 15 seconds to complete, with a pain rating of 9/10. Five times sit-to-stand test completed in 20 seconds with NRS pain 8, NRS fatigue 7.

Assessment Considerations

In this case, self-reported pain is assessed at rest and with movement. This strategy was used because the therapist determined the MPQ would consume treatment time, which could be used in a more productive way. Impairments of ROM, strength, and palpation are supported with PPT assessment at the knee as an indicator of peripheral involvement and lower leg to assess potential central changes. The WOMAC and SF-36 questionnaires were chosen for a disease-specific assessment and a generalized quality-of-life assessment of pain on physical and mental function. The painDETECT was chosen on the basis of her high pain complaints and that a proportion of those with osteoarthritis have neuropathic pain. The TUG was used to assess ambulation/function specifically to decrease the chance of exacerbation of knee pain that is suspected to occur with the 6MWT. The 5TSTS test was chosen to assess repetitive knee flexion in the weight-bearing position and lower limb strength because her worst pain intensity rating (7/10) associated occurred with stair climbing. Screening questions for depression and anxiety are used because of the chronicity of the condition and her expressed concern over continuing her job. If the patient demonstrates fear of worsening symptoms with a prescribed exercise program, the TSK or FABQ could be used at a subsequent visit.

Case 10

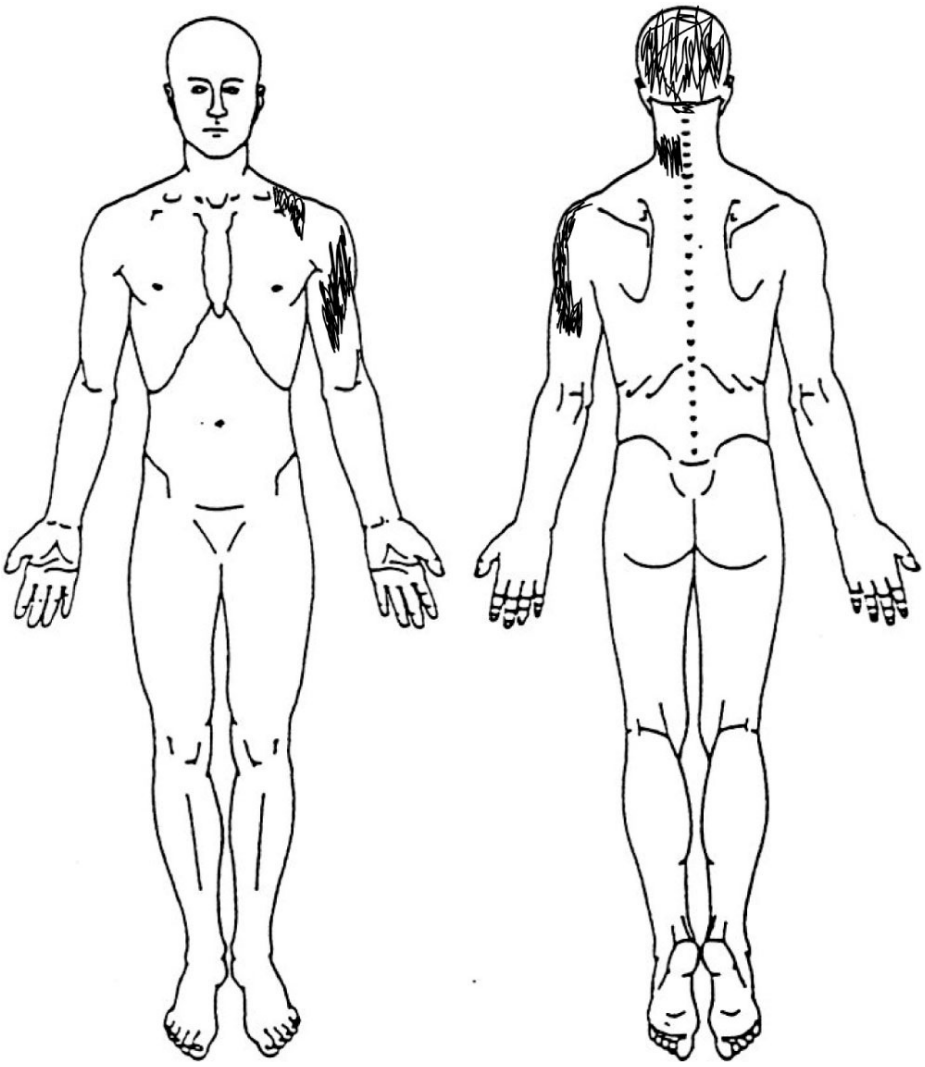
Subjective Assessment

This patient is a 43-year-old woman who has had neck pain for 5 months, with no other medical problems. She has not seen a physician or any other health professionals for her neck pain. She had prior experience with physical therapy for her knee that she found very helpful in the past and thought she would come first to the physical therapist. Pain started after she rotated her neck at work to one side and felt a sharp twinge on the left side. Her pain is now an ongoing aching pain on the left, with sharp pain when she moves her neck too fast. Her pain is worse at the end of the day. She gets occasional headaches that start in the back of the head and radiate to the front. She states that she has had these types of headaches for years, but they are more frequent now, occurring at least once a week. She also has aching in her left shoulder and upper arm on "bad days." She works as a technical writer, spending most of her time at a computer during the day. She continues to work but is unable to do activities at night. Lying down on her back makes the pain better. When asked, she denies nausea, dizziness, blurred vision, fever, sweating, or changes in bowel or bladder habits. When asked, "Is there anything else going on with your body at this time that we have not discussed?" the patient reports she has some left knee pain if she sits too long or climbs stairs.

Medical history screen is positive for 5-year history of type II diabetes mellitus controlled with medication and diet. The patient has not traveled out of the country in the last 5 years. There is no evidence of a red flag history or risk factors reported (injury to head, neck or face, sore throat, skin rashes, increased pain with exertion, night pain, jaw pain, visual disturbances, seizures, or blacking out).

Headache Screening Questions
Do your headaches wake you up when sleeping? No
Insidious or new onset of headache in last 6 months? Yes
Previous history (personal or family) of migraine? No
Headache associated with changes in blood pressure? Don't know
Headache associated with blacking out? No
Headache associated with flu-like symptoms or jaw pain? No
Headache associated with confusion? No
Headache associated with neck stiffness? Yes

Case 10



Pain Assessment

McGill Pain Questionnaire: Words chosen: throbbing, sharp, cramping, aching, tender, troublesome, nagging. PRI-S: 13/42; PRI-A: 0/14; PRI-E: 1/5; PRI-T: 17/78. Current neck pain on VAS: sensory-discriminative scale: 4/10; motivational-affective scale 2/10.

Questionnaires
PHQ-2 (Table 24-3): 1/6
GAD-2 (Table 24-3): 0/6
PSEQ (Table 24-1): 51 demonstrating minimal deficits with only concerns for leading an active lifestyle
SBST: 2/9
painDETECT: 4

Objective Assessment

Resting vital signs: HR 62, BP 124/76, RR 14.
Active ROM: shoulder and lower back normal. *Cervical ROM*: flexion: P1, 3 inches from chest; P2, full, to chest. Extension: P1, 30 degrees; P2, 45 degrees (full ROM). Rotation, right: P1, 10 degrees; P2, 40 degrees (patient stops because of stiffness). Rotation, left: P1, 70 degrees; P2, 80 degrees. The patient has increased pain with cervical flexion.
Neurological exam: reflexes normal, brisk, and symmetrical; localized light touch: within normal limits at C1–T1 bilaterally; manual muscle testing of upper extremity: within normal limits bilaterally.
Palpation: tenderness located from C3 to T1 bilaterally next to the spine. Tenderness is also located over the upper trapezius on the left, and the pain is referred to the base of the skull. Muscle spasms are felt with palpation of the left cervical spine from C4 to C7.
Special tests for upper cervical instability (vertebral artery test, sharp purser, cervical distraction, and anterior shear) were all negative.
Sensation: Monofilament exam of the plantar aspect of both feet indicates no loss in protective sensation with patient able to consistently detect the 10 g monofilament.

Assessment Considerations

Medical history screening and the outlined screening questions are included in this case to remind therapists of the importance of screening for diagnoses that require referral to another medical provider. Additional questions relating to headaches are included to screen for red flag symptoms associated with headache that require referral to a physician. The painDETECT was chosen because of the presence of referred pain to the shoulder and does not indicate neuropathic symptoms. The SBST was chosen because of the chronicity of the pain. Both of these tools were also chosen because of the direct access presentation of the patient to physical therapy in the absence of examination by the physician. The assessment of P1 and P2 assesses the irritability of movement to determine how aggressive the plan of care should be. In this case, the patient presents with minimal irritability. The monofilament exam was conducted because of patient's current condition of type II diabetes mellitus and the special tests of the cervical spine were employed to assess upper cervical instability and potential for immediate referral to a physician. With negative screening results for anxiety and depression and painDETECT, the MPQ, self-efficacy screen, and

SF-36 provide the therapist sufficient information when added to the traditional impairment measures (ROM, MMT, palpation, neurological exam) to initiate the plan of care. Additional multidimensional disease-specific assessments may only increase patient burden. If signs of depression, anxiety, or fear of movement become part of the picture, the therapist can employ the use of additional assessments as presented in the previous cases.

SECTION 2: GENERAL CONSIDERATIONS AND TREATMENT

Case 1

General Considerations

The patient appears to have pain that is driven primarily from a peripheral component with potential neuropathic symptoms (Table 24-4). The referred pain indicates involvement of the central nervous system. She marks an additional area in the thoracic spine on the body diagram and thus the clinician should keep awareness of the potential for widespread pain. However, because the pain centralizes with extension, that is, there is a reduction in leg pain with standing in extension, lying supine, and prone positioning, it suggests the central component is driven by mechanical factors from the peripheral nervous system. He also has increased symptoms with flexion of the lumbar spine, altered posture, pain in the back, and reduced ROM as a result of pain, all of which are difficult to determine mechanisms for the underlying pain. He appears to have signs of radiculopathy because he has diminished sensation and accompanying pain in the posterolateral aspect of his leg, although his strength and DTR are normal. His painDETECT score of 18 suggests that further evaluation is warranted. Imaging studies show signs of bulging disks and not herniated disks, suggesting minimal compression of the nerve root. Further bulging disks are common in asymptomatic individuals, and do not often correlate with symptoms in individuals with low back pain (see Chapter 19). The lack of changes in DTR and strength, and minimal changes on imaging, despite the loss of sensation in the lower leg, suggest minimal neuropathic pain. The pain is recurrent, and this bout has lasted for 4 months, and thus we must consider the involvement of central factors that may contribute to the pain. However, the self-efficacy questionnaire shows minimal deficits, with the greatest deficits in socialization,

hobbies and leisure activities, and coping. Quality-of-life assessment shows minimal decreases in physical functioning and no change in mental health function. The SBAT scores indicate the patient is at low risk for a poor prognosis. Together, these tests (yellow flag screening, Chapter 19) do not indicate psychosocial concerns for this patient.

Treatment

The therapist will proceed with treatment with the understanding that the patient will be referred to the physician for further evaluation of the neuropathic signs and symptoms. Based on the evaluation the patient has nonspecific low back pain that can be further subgrouped into “chronic LBP with radiating pain” (Chapter 19).

The pain is substantially lessened with extension, and worsened with flexion, so the focus should be on a specific exercise program aimed at centralizing pain to the lower back (extension exercises). The Orthopedic Section of the American Physical Therapy Association states there is strong evidence for use of centralization and directional preference exercises (Chapter 19). Other exercise programs, particularly trunk coordination, strengthening and endurance exercise, as well as aerobic conditioning exercises, also have strong support for individuals with chronic low back pain (Chapters 10 and 19). The patient continues to exercise at a fitness center three times per week, so you should discuss this program to ensure that it includes an aerobic conditioning program and proper weight-lifting techniques that do not strain the back.

All physical therapy treatments should also include an educational program, which is standard of care for all chronic diseases. The educational program will support the exercise program and improve adherence. For this patient, education should be focused on the patient taking an active role in the management of his condition. Components that might be helpful for this client would include patient education on pain, disease and assessments, pacing and coping skills, and pain management with nonpharmacological approaches (see Chapter 9). Understanding of “hurt verses harm” and factors that improve or worsen the condition should be reviewed. There is weak to moderate evidence for education for people with chronic low back pain (Chapters 9 and 19).

If education and exercises alone do not improve symptoms and pain within the first week, pain control techniques should be added. These could include transcutaneous electrical nerve stimulation (TENS), physical agents, or joint mobilization/manipulation. Using TENS or joint manipulation for pain reduction could produce effects in the central nervous system geared to reduce central

sensitization. At present, evidence from Cochrane reviews does not support the use of TENS for chronic low back pain, but a meta-analysis suggests TENS is effective for chronic musculoskeletal pain conditions including low back pain (Chapter 11). Heat therapy has moderate evidence for effectiveness in individuals with low back pain (Chapter 12). Massage shows improvements over sham for pain relief, and spinal manipulations and mobilization have a small effect on chronic low back pain (Chapter 13). TENS, heat, and manual therapy all produce short-term effects on pain, and are thus generally used as adjunct treatments to an exercise program.

Lastly, if centralization-specific exercises and the addition of pain-reducing treatments are still not effective, the addition of psychological treatment aimed at teaching coping skills could benefit this patient, or a multidisciplinary approach should be considered. However, this is not a first choice on the basis of the screening tools used that show minimal psychosocial concerns.

Case 2

General Considerations

This patient has evidence of both peripheral and central components to her pain (Table 24-4). She has had a clear peripheral injury, that is, fracture, with loss of motion and strength due to immobilization all pointing to peripheral mechanisms underlying her pain. The malaligned wrist suggests that you may not be able to restore full ROM but will focus on regaining functional ROM. The allodynia to cold and touch (inability to tolerate cold and gloves), decreased temperature of the hand, guarding, positive Von Frey examination, joint swelling, and stiffness suggest that she has complex regional pain syndrome (CRPS) as a result of a fracture followed by immobilization. CRPS and allodynia are centrally mediated. The TSK and PCS scores indicate the patient is at risk of complications and poor outcomes associated with fear of movement and catastrophizing, and thus the patient has psychological concerns that need to be addressed with treatment. If patient education directed to address these risks fails to provide acceptable progression toward goals in the preliminary visits, a multidisciplinary approach should be considered. The painDETECT score of 8 suggests the patient does not have significant neuropathic contributions to her pain.

Treatment

Initial treatment will start with an education and self-management program. This education program will be comprehensive discussing the biological processes underlying pain using Explain Pain techniques as well as disease-specific education about the fracture, healing, and CRPS. The self-management program will also work with patient-specific goals developed in collaboration with the patient, and the clinician will educate on realistic and attainable goals as well as how to modify goals throughout the course of treatment. Further, the therapist will work with the patient to write out an active management plan that includes a home exercise program (Chapter 9). It will be particularly important to address the fear of movement and the pain catastrophizing in this patient using explanations provided by Explaining Pain, hurt versus harm, value of exercise and use of the arm, and coping and pacing skills. There is weak to moderate evidence for education programs for individuals with chronic pain and randomized controlled trials (RCTs) showing efficacy of Explaining Pain for individuals with CRPS and neuropathic pain (Chapter 9).

An active exercise program will be initiated with the goals of increasing ROM and strength of the wrist. Initial exercises will begin with active ROM, progressing, as permitted, to light strengthening exercises for the wrist and hand. Exercise has been shown effective for a variety of pain conditions and is standard of care after fracture with immobilization (Chapter 9). Active exercise is also part of evidence-based guidelines for those with CRPS, and RCTs show efficacy for CRPS (Chapter 21). In addition, mirror therapy or desensitization therapy will be added to the treatment plan to improve pain and symptoms of allodynia and reduce guarding of the limb. RCTs show efficacy of mirror therapy and desensitization therapy for CRPS (Chapter 21). Further, an aggressive exercise program can also decrease fear of movement and disability, and improve function and quality of life (Chapter 21).

For treatment of the pain and stiffness, thermal modalities (such as whirlpool, paraffin wax, or fluidotherapy) will be used prior to the active exercise program (Chapter 12). The patient will be instructed in the use of warm water baths at home before performing her home program of active ROM exercises (Chapter 9). There is minimal evidence for use of physical agents for this type of pain or stiffness. Effects of heat therapy are expected to be temporary but may assist the patient in participation in the exercise program.

Once the allodynia is reduced or eliminated, the therapist will assess for hypomobility of the wrist and hand. Treatment will then include joint mobilization to regain ROM, as indicated by the evaluation for hypomobility. Both dynamic and passive joint mobilizations will be performed.

It will be important to coordinate treatment with the physician to ensure that

proper pharmacological treatments for CRPS are given at the same time as physical therapy. A number of pharmacological options are available for the treatment of CRPS (Chapters 15 and 21). Further, as the TSK and PCS are significant, a multidisciplinary approach that not only includes pharmaceutical management and physical therapy but also adds psychological management could be beneficial and is recommended if the patient does not respond to the current plan of care (Chapter 14).

Case 3

General Considerations

This patient has lateral epicondylalgia, and a mixture of both peripheral and central mechanisms probably underlie his pain (Table 24-4). Evidence for peripheral mechanisms includes localized pain, and pain on palpation at the primary site of pain. However, the year-long duration of the pain, the unrestricted but painful accessory joint movements, the fear of using the arm at work and high TSK values, and the minimal effects of NSAIDs and local injections all suggest a central component to his pain. His self-efficacy questionnaire (CSPS) and quality-of-life survey have significant deficits in all aspects, including coping skills and the ability to do chores, socialize, and work. The McGill Pain Questionnaire shows that the patient has chosen aspects related to all three dimensions of pain. Therefore, this patient has significant psychological concerns that will need to be addressed, and may interfere with progress.

Treatment

Initial treatment will be aimed at a comprehensive education program focusing on the underlying mechanisms for the pain (Explaining Pain), hurt versus harm, and ways in which he can use the arm during work and leisure activities without putting stress on the joint and soft tissues. As this patient is a dentist, it will be possible to give a more in-depth education on the disease and the neurobiology of pain. A self-management program will also work with patient-specific goals developed in collaboration with the patient, and the therapist will work on the patient to write out an active management plan that includes a home exercise program (Chapter 9). It will be particularly important to address the fear of movement and low self-efficacy focusing on principles of Explaining Pain, hurt

versus harm, and coping and pacing skills. There is weak to moderate evidence for education programs for individuals with chronic pain and RCTs showing efficacy of Explaining Pain and self-management programs in some musculoskeletal pain conditions (Chapter 9). Involving the patient in setting attainable short-term goals directly relating to his situation and desires will be used to improve overall adherence to the multipronged intervention approach.

While the patient is at work, you will have the patient wear a wrist cockup splint to maintain neutral wrist extension until the patient can maintain this position without the splint. This will allow the patient to reduce the stresses on the joint during work activities. The brace will also be used in any instance where he begins to feel the low-grade aching begin. The patient would benefit from an exercise program aimed at improving strength of the upper extremities, with an emphasis on wrist extension and hand strength, to regain function of the arm. Evidence from a systematic review shows that strengthening exercises for lateral epicondylalgia reduce pain at rest and during activity [3].

To reduce pain from lateral epicondylalgia in this patient, you will add local mobilizations of the elbow, as well as TENS, which will activate central inhibitory mechanisms aimed at reducing the central components of the pain. Evidence from systematic reviews suggests that mobilization of the elbow for people with lateral epicondylalgia decreases pain (see Chapter 13) and that TENS reduces pain associated with chronic musculoskeletal pain (Chapter 11). Low-level laser therapy may also be a choice as systematic reviews show efficacy in reducing joint pain (Chapter 12), and ultrasound is effective for tendonitis (Chapter 12).

Because the pain is of long duration, and the patient has significant deficits in self-efficacy and quality of life, and assessment shows potential for depression and anxiety to be concurrent with the condition, a multidisciplinary treatment program should be started. This program should include coordination of services with a physician and psychologist specializing in pain management. Pharmacological management can also add to the treatment of this patient, particularly with drugs directed to the central nervous system sensitization (Chapter 15). The therapist should directly contact the physician with concerns about depression and anxiety, and carefully monitor progress to see if referral to a psychologist is necessary. Evidence from systematic reviews suggests that multidisciplinary treatments that involve physicians, nurses, physical therapists, and psychologists can improve pain and function in people with chronic pain (see Chapter 14). There is also evidence that cognitive-behavioral treatment improves pain in a variety of chronic pain conditions (see Chapter 16).

Lastly, this case demonstrates the importance of screening for anxiety and

depression in all patients. This dentist did not present with any such signs in the subjective interview; yet the results of the two-question screening tools (PSQ-2 and GAD-2) revealed significant concern about depression and anxiety prompting the therapist to refer back to the physician or a psychologist. It may be useful to add additional screens such as the TSK or PCS at subsequent sessions. Even when these screens are negative they provide a baseline that can be used to monitor psychological status over time.

Case 4

General Considerations

This patient's pain is primarily central in nature, but has resulted in tightening of the shoulder capsule in a capsular pattern and thus now also has a peripheral component to the pain (Table 24-4). Signs of central mechanisms include insidious onset and pain lasting more than 6 months without relief from standard treatments aimed at reducing peripheral inflammation (NSAIDs and local injections). The patient has referred pain, that is, pain radiating into the forearm, and this radiating pain increases with movement. This patient's body diagram indicates multiple areas of pain not related to the primary complaint at the left shoulder, that is, widespread pain. Peripheral signs include loss of ROM from the tightened shoulder capsule, localized shoulder tenderness, and localized pain. Her pain significantly affects her function and ROM. Peripheral components include the apparent tightening of the joint capsule with loss of motion and localized pain to the shoulder. She does not appear to have neuropathic components to her pain. She has significant impairments in all areas of the self-efficacy and quality-of-life questionnaires, and the McGill Pain Questionnaire shows aspects of all three dimensions of pain suggesting psychological concerns that need to be addressed.

Treatment

As this is a mixed condition with both peripheral and central components to the pain, along with psychological concerns, a comprehensive treatment plan will be used. Patient education will be most prominent in the initial treatment sessions and persist throughout treatment such that at discharge the patient is equipped with self-management strategies. The emphasis on the importance of short-term goals that are specifically important to the patient, benefits of exercise and

movement, as well as examples of hurt versus harm should be employed. Employing Explaining Pain principles, coping skills, and pacing will be important for this patient to address her fear avoidance and catastrophizing concerns (Chapter 9). Additionally, her physician should be contacted to discuss the scores on the anxiety and depression screening, and the patient should be consulted in discussing these concerns with her doctor or a psychologist (Chapters 6 and 14). Because of the chronic nature of the pain, the significant impact on function and daily activities, and the psychological concerns in this patient, a multidisciplinary approach that includes coordination of services between a physician, psychologist, and a physical therapist would likely produce the greatest results and should be used (Chapter 14). Evidence from systematic reviews suggests that education, cognitive-behavioral therapy, and multidisciplinary treatment are effective in reducing chronic pain and improving function (Chapters 9 and 14). Although there is strong evidence suggesting that corticosteroid injections for adhesive capsulitis improve pain and function [2], this initial approach was not successful in this patient.

Physical therapy treatments will be aimed at improving ROM and function of the arm, and at modulating central nociceptive processing. The current evaluation shows that the patient has significant pain (7/10 at rest and 9/10 with movement), and thus initial treatments must be aimed at reducing this patient's pain scores. This can be done by using treatments such as TENS (alternating between low and high frequencies) to activate central inhibitory mechanisms (Chapter 11). As TENS produces greater effects on movement pain when compared with resting pain, TENS will be used during an exercise program and during work to allow the patient to participate in daily activities and exercise (Chapter 11). Evidence from a meta-analysis shows that TENS reduces pain in chronic musculoskeletal conditions (Chapter 11). Alternating between low- and high-frequency TENS will activate both μ-and δ-opioid receptors to improve pain reduction and reduce tolerance with repeated use (see Chapter 11). Alternatively, the use of heat or ice could also provide temporary relief of pain to allow the patient to perform an exercise program. Evidence for use of heat and cold is weak, and they provide short-term relief of pain. However, the patient can be educated on the use of these agents at home to facilitate participation in a home exercise program (Chapter 12). There is weak evidence from guidelines by the Orthopedic Section of the American Physical Therapy Association for combining electrophysical agents with exercises for adhesive capsulitis [2].

Initial exercise treatments will start slowly with increasing active ROM through stretching. Once the pain has decreased to a moderate level, a more progressive exercise program will be instituted aimed at increasing strength of

the shoulder, and a walking program to encourage normal arm use, to reduce guarding, and to activate central inhibitory mechanisms to reduce pain. Additionally, aerobic exercise is effective for treatment of chronic pain conditions with a central component such as chronic low back pain and fibromyalgia (see Chapter 7). Increasing ROM with an active exercise program is expected to increase the available ROM and reduce the mechanical irritant and the activation of nociceptors in the shoulder and is recommended in clinical practice guidelines on the basis of moderate evidence [2].

Joint mobilizations of the shoulder will be added after the patient is actively participating in her rehabilitation program to decrease any remaining hypomobility of the shoulder. Joint mobilizations will similarly be used to increase the active ROM and reduce the mechanical activation of nociceptors in the shoulder (see Chapter 13). While there is limited evidence for the use of peripheral joint mobilizations in pain conditions, but clinical practice guidelines recommend mobilization of the shoulder joint to improve motion and reduce pain in those with adhesive capsulitis [2]. Joint mobilizations may not only improve ROM to reduce a mechanical irritant on nociceptors, they also have a central mechanism of action that reduces central excitability and activates central inhibitory pathways (Chapter 13).

Case 5

General Considerations

The patient's pain in this condition probably results primarily from peripheral mechanisms (Table 24-4). The pain is reproduced with pressure on the buttock and is relieved by stretching, which suggests myofascial pain. She has reduced motion in internal rotation of the hip, as well as reduced strength and pain in external rotation of the hip. All other movements are within normal range. Although she has symptoms of referred pain, these symptoms can be reproduced by pressing on the trigger point, suggesting that the referred pain is of myofascial origin and driven by activation of peripheral nociceptors. The painDETECT, SBST, SF-36, self-efficacy results, and depression and anxiety screening question together suggest that the patient does not have neuropathic pain and that there are no psychosocial concerns. Her Oswestry, 6MWT, and 5TSTS scores are low compared with age-matched controls, and her HR and BP responses are within normal limits and estimate attainment of 60% age-predicted MHR. These functional assessments and the objective measures suggest that the

myofascial pain will be the focus of her plan of care. Special tests for spine pathology and biomechanics consume time and may not yield additional information to direct the intervention in this chronic pain condition.

Treatment

Treatment of this individual will be coordinated with a physician who will give trigger point injections, or the therapist will perform dry needling. There is strong evidence that dry needling decreases pain intensity and improves ROM, and that lidocaine trigger point injections are superior to dry needling (Chapter 17). Physical therapy will begin immediately after this injection, with active ROM and stretching in combination with ischemic pressure (trigger point massage) over the trigger point in the piriformis muscle. Evidence from RCTs shows that active ROM and stretching exercises, combined with ischemic pressure manual therapy, reduce pain in people with myofascial pain syndrome (see Chapter 17). If this treatment approach is ineffective, the addition of electrotherapy, either interferential or TENS, should provide pain relief and is supported by RCTs (Chapter 17). Because the patient has a sedentary job and does not participate in regular physical activity, a walking, swimming, or aerobic exercise mode of choice will be prescribed to allow an overall activation of central inhibitory mechanisms (Chapter 10). Education will be geared toward understanding the nature of pain, the benefits of exercise for pain control, and self-management techniques (Chapter 9).

Case 6

General Considerations

This patient appears to have pain that is driven primarily from a central origin, with a probable diagnosis of fibromyalgia (Table 24-4). Signs of centrally driven pain include the duration of pain greater than 1 year, widespread pain, fatigue, and sleep disturbances. She also has significant psychological concerns as evidenced by the screening questionnaires, TSK, PCS, and self-efficacy scores, and together these assessments suggest that her pain affects all aspects of her life, from physical functioning to mental health.

Treatment

A referral to her medical provider (family physician, rheumatologist, internist) should be made to confirm the fibromyalgia diagnosis and to start on a comprehensive pain management program. For this patient, the result of the FIQR was 77, which indicates rather severe disease impact (0–100 scale). Treatment of this patient must be multidisciplinary and would be best managed in a multidisciplinary pain center. Treatment will include coordination of services from pain management specialists in medicine, nursing, psychology, and physical therapy. There is strong evidence for a multidisciplinary approach for people with fibromyalgia (Chapter 17). There is also strong evidence for several pharmacological classes of drugs, mainly antidepressants and anticonvulsants, in this population (Chapter 17).

The physical therapy treatment approach will be an active aerobic exercise program starting with only 2–3 minutes of walking two to three times per day because the patient was unable to complete the 6-minute walk test. The long-term goal will be to reach 20–30 minutes of daily walking in one session. The patient will be progressed slowly, with an emphasis on success, which may include increases as small as 1 min/d. A strength training program will be added once the patient is actively participating in the aerobic exercise program and has made significant progress toward the goals. The strength training program will emphasize trunk muscles and proper postural support. A Cochrane systematic review and evidence-based clinical practice guidelines for fibromyalgia show strong evidence for aerobic conditioning exercises to reduce pain and improve function (see Chapters 10 and 17). Moderate evidence from the Cochrane review and evidence-based clinical practice guidelines exists for the use of strengthening exercises for people with fibromyalgia (see Chapters 10 and 17).

A self-management program that includes education and is reinforced by psychological management is essential in these patients. As this is a chronic disease, it is essential that patients learn to manage their pain on a day-to-day basis. Working closely with the psychologist, and physician, to coordinate self-management goals will provide the most successful results. The program will include patient education on pain and disease, movement, activity and pacing, management skills with nonpharmacological approaches, and development of coping skills. Thus, through self-management and education, along with an exercise program, we aim to make the patient an active participant in the -management of their condition by giving them the skills to master their own situation (Chapter 9).

If necessary, electrotherapy or massage can be added to help reduce the pain (1) once the patient is actively participating with the aerobic conditioning program or (2) prior to exercise to decrease pain and allow her to increase her

exercise levels. Both electrotherapy and massage are expected to have short-term effects in this population and are thus used as an adjunct to facilitate participation in an active treatment program. Recent evidence from RCTs shows that TENS in individuals with fibromyalgia can reduce pain, particularly movement pain (Chapters 11 and 17), and a systematic review shows that massage can improve pain, anxiety, and depression in individuals with fibromyalgia (Chapter 13).

Case 7

General Considerations

This patient has an acute ankle sprain with inflammation of the joint and associated pain and thus has pain likely driven by nociceptor activation (Table 24-4). There are likely to be increases in inflammatory cytokines, prostaglandins, and tumor necrosis factor, which are activating and sensitizing nociceptors. In addition, inflammatory neuropeptides, substance P, and calcitonin gene-related peptide are probably contributing to the inflammation by enhancing plasma extravasation and vasodilation, and by activating noninflammatory cells to further enhance the release of inflammatory substances into the joint. The pain is probably a direct result of nociceptor sensitization (see Chapter 2). Signs of a peripheral component to the pain are the acute injury, local pain, pain with pressure over the ankle, and swelling. Of note, though the patient is in the subacute phase of inflammation and repair, he would be classified as an acute pain patient. The patient also has referred pain, as evidenced by radiating pain into the calf and lower leg on occasion; however, this is likely being driven by the peripheral inflammation and is a normal response to an acute injury. There are no signs of neuropathic pain. The results of the SBST screen indicate this patient is at low risk for a poor prognosis, and there are no additional psychological concerns from the anxiety or depression screening questions.

Treatment

Treatment with pharmacological agents for reduction in inflammation and pain will be managed by the physician and could include NSAIDs and weak opioids (Chapter 15). Physical therapy treatment for this patient will include education and self-management, exercise, and physical agents. The self-management program will include education on home use of ice and elevation to decrease

inflammation and reduce pain, use of a brace and/or crutches to improve gait quality, protect the joint, and limit the potential of negative motor adaptations (Chapter 4). Time frames for tissue healing will be emphasized in relation to appropriate activity level advancement. Treatment interventions will generally be aimed at reducing the peripheral inflammation and pain with local treatments, as well as increasing pain-free ROM. He will be instructed in an active ROM program to maintain and increase movement in the ankle, and the home use of physical agents and elevation. The intermittent referred pain will most likely be resolved with removal of the peripheral irritants, and the patient has good prognosis. Systematic reviews show limited evidence for ice in reducing inflammation and improving pain, and these effects are of short term (see Chapter 12). There is no evidence at present to suggest that active ROM exercises in acute pain will maintain ROM and improve function in the long term. However, general principles of physical therapy for acute injury are aimed at maintaining function and reducing the pain associated with the acute injury. If ice and ROM exercises do not produce a desirable reduction in pain and inflammation, then one can try electrotherapeutic modalities, such as TENS, for pain or high-voltage electrotherapy to reduce inflammation and pain. Basic science evidence shows that TENS can reduce hyperalgesia associated with acute inflammation and a recent Cochrane review shows effectiveness for TENS in acute pain (Chapter 11).

Case 8

General Considerations

This person’s pain is primarily maintained by central mechanisms (Table 24-4). Signs of central involvement include referred pain into the hip, leg, and upper back, initial normal imaging and tests after the injury, the duration of the pain, inability to work, tenderness over the hip and upper back, difficult concentrating, and fatigue. Central changes are also supported by widespread pain documented in the body diagram. She has significant deficits in self-efficacy, reduced quality of life in all domains, and high scores in all three dimensions of the McGill Pain Questionnaire. Peripheral signs are few, but they might include tenderness over the lower back, postural changes, and muscle tightness and weakness. However, this patient’s peripheral components could be a direct result of long-term deconditioning, poor posture, and guarding as a result of the pain. It is likely that these peripheral components are secondary to the pain condition. Finally, the

blood pressure response to exercise (>20 mm Hg increase in systolic blood pressure [SBP] and 10 mm Hg increase in diastolic blood pressure [DBP] with testing) should be reported to her physician for further evaluation.

Treatment

On the basis of the multiple pain areas on her body diagram, the long duration of the pain, and the strong psychological concerns, this person is best treated with a multidisciplinary program that would include medicine, psychology, nursing, physical therapy, and potentially vocational rehabilitation. Goals for treatment will be to treat the strong central component to the pain, and to engage the client as an active participant. As a member of the medical team, the physical therapist will coordinate all treatments with those of other disciplines through team meetings. Evidence from systematic reviews shows that multidisciplinary treatment is more effective than single-disciplinary standard care for the treatment of chronic low back pain to improve function and decrease pain (Chapter 14). Evidence-based guidelines suggest the use of certain pharmacological agents such as benzodiazepines, antidepressants, and tramadol, which have moderate to strong efficacy (Chapters 15 and 19). Cognitive-behavioral treatments also have strong evidence to support their use in people with chronic low back pain (Chapters 16 and 19).

Physical therapy treatments will focus on a self-management program that includes education, coping skills, and active exercise. This patient is the ideal candidate for a comprehensive exercise program geared toward a better understanding of pain processing in the peripheral and central nervous system using the Explaining Pain conceptual framework (Chapter 9), and coping and pacing skills. The patient will be educated on the data showing a lack of correlation between imaging results and pain, and that the imaging results even for herself were normal after the accident and changed over time, a normal process of aging. Education will also include sleeping hygiene and posture, and movement strategies to reduce pain and fatigue. Emphasis will be placed on the patient taking an active role in the management of their pain condition. Data from systematic reviews show weak support for education in the management of chronic pain (Chapter 9); however, education is considered an integral part of evidence-based guidelines for individuals with chronic pain (Chapter 19).

Physical therapy treatments will also include active exercise program using both spinal stabilization exercises and aerobic conditioning exercises. Data from systematic reviews and clinical practice guidelines show that spinal stabilization and aerobic conditioning exercises in a supervised setting show strong evidence

for decreasing pain and improving function in people with chronic low back pain (see Chapters 10 and 19). If pain and function do not improve significantly with this treatment approach, joint mobilization, massage, or electrotherapy should be added. These additional strategies, which are passive treatments, will only be added when the patient has made a commitment to take part in an active exercise program. There is also evidence from clinical practice guidelines and systematic reviews that joint manipulation is effective for chronic low back pain (see Chapters 13 and 19), and from one meta-analysis that electrotherapy is effective for chronic musculoskeletal pain conditions but it has not shown to be effective for chronic low back pain (see Chapter 11). The research on TENS effectiveness for low back has been questioned on the basis of adequate dosing, timing of assessment, and type of outcome assessment used (see Chapter 11 for discussion).

Case 9

General Considerations

The patient has knee osteoarthritis with degenerative changes that are producing pain. The pain is clearly associated with peripheral changes in the joint, but the pain (9/10 during movement) is out of proportion to the degree of changes in the joint (Grade II osteoarthritis). Thus, she probably also has significant central sensitization that will need to be addressed to get adequate treatment results (Table 24-4). Central changes are also indicated by the decreased PPT in the lower leg as compared with the contralateral leg. She has a score of 20 on the painDETECT, indicating that she likely has neuropathic symptoms contributing to her pain. Screening questions for depression and anxiety do not suggest the immediate referral for psychological intervention; however, the therapist should remain watchful for reassessment and referral if treatment progresses without significant progression toward mutually set short-term goals. Treatment should be aimed at both peripheral and central mechanisms to relieve pain and improve function. The patient's function and quality of life in the physical domains are significantly compromised. The patient has difficulty working, performing household chores, and performing general self-care (bathing and dressing). TUG and 5TSTS tests suggest decreased function associated with strength and general mobility.

Treatment

The patient is currently being managed by a rheumatologist for osteoarthritis and is receiving pharmacological management for her pain. A discussion with the physician about the severity of pain and its impact on function should be initiated. Her physical therapy intervention program will be aimed at (1) gaining a better understanding of pain processing and osteoarthritis, through education; (2) developing self-management strategies for the pain; (3) increasing the strength of the knees through an active strengthening program; and (4) increasing function through a general aerobic exercise program that puts minimal stress on the knee joint, such as aquatic therapy or a stationary bicycle. There is strong evidence from systematic reviews that strengthening and/or aerobic conditioning exercises in people with knee joint osteoarthritis can decrease pain and improve function (see Chapters 10 and 22). This evidence suggests that there are equal effects with strengthening, land-based or aquatic-based therapy, or with group therapy, and thus any type of exercise program should be considered and assessed for each individual patient. Because the patient has significant pain with walking (during the timed up-and-go test) you will also add pain relief with high-frequency TENS and educate the patient on the use of heat and cold therapies at home for pain reduction. There is mixed evidence from systematic reviews that high-frequency TENS reduces pain associated with osteoarthritis of the knee. Systematic reviews that use adequate intensities of TENS for osteoarthritis show positive results in the clinically significant range [1] (see Chapters 11 and 22). Although there is minimal evidence to support the use of heat and cold for arthritis, thermal modalities are recommended for palliative care in systematic reviews. Further, they have minimal side effects, can be done by the patient at home, and probably have short-term effects (see Chapter 12). You will also include education on weight control and on avoiding excess stress on the joint during activities of daily living. The temporary use of a single-tip cane may be explored with education of decreasing weight-bearing joint forces in the short term. To manage expectation of decreased pain and improved function as a result of an active exercise program, you will educate the patient about dedication to daily exercise for 3–4 weeks before expecting significant change, and that continuation of exercise will be required. It may be beneficial to discuss the underlying pain neurobiology using an Explaining Pain approach focusing on changes in pain outside the primary site (knee) for the patient to appreciate the central changes that have occurred and why simply using treatments directed at the knee may not address the entire problem. There is minimal evidence to support an education program and good evidence to support cognitive-behavioral therapy in osteoarthritis (Chapters 9 and 22). Finally, because her anxiety screening score is borderline, a

repeat screen should be administered after 10–14 days of intervention to assess for changes in either direction, with subsequent follow-up as indicated. Administration of additional psychological assessments such as the TSK, FABQ, PCS, or self-efficacy questionnaires should be considered. Clinical studies suggest that anxiety, depression, fear of movement, pain catastrophizing, and high pain levels particularly during movement are risk factors for poor prognosis in osteoarthritis and after total knee replacement (Chapter 22). Thus, you will pay close attention to these modifiable risk factors to examine for improvements or to modify your treatment plan accordingly. Low-level laser therapy could be an alternative treatment as systematic reviews show reductions in pain with optimal doses (Chapter 12).

Case 10

General Considerations

This patient has signs of primarily central sensitization, which include long duration of pain, normal muscle strength, and referred pain to the head, arm, and shoulder. Her ROM shows minimal decreases but is painful (Table 24-4). Several factors suggest that the pain is not irritable and that treatment can be more aggressive: (1) a minimal difference between P1 and P2; (2) minimal limitations in ROM, and normal strength; (3) a minimal affective component to the pain (2/10 on VAS, 0 on the McGill affective scale); (4) limitation in rotation on the right side as a result of stiffness, and not pain; (5) absence of neurologic signs. She does have limited ROM in rotation to the right because of stiffness, suggesting soft-tissue tightness that may limit movement. Her tension-type headaches are long-standing and appear to be aggravated by the neck pain. However, the results of HA screening indicate she would benefit from referral to determine if hypertension is associated with these more frequent headaches, which may be concurrent with her neck problem, not directly associated with it. Her quality of life is good, her anxiety and depressions screens are negative, and she has high self-efficacy, indicating she should respond well to treatment.

Treatment

Given that the patient presented to you without seeing a physician, you must first consider if referral is appropriate. Her quality of life is relatively normal, her self-efficacy is high, she shows moderate pain on the sensory-discriminative

dimension (McGill Pain Questionnaire and VAS), and there is minimal to no motivational-affective component to the pain, suggesting that this patient is coping effectively with the pain at this time. Her depression and anxiety screens are negative and offer a baseline for future assessment across time in this chronic pain case. She does not appear irritable and has no “red flags” (normal neurological examination and no constitutional symptoms) on evaluation. Her STarT back screen is negative for poor prognosis as is her painDETECT score to screen for neuropathic pain. As such, the course of treatment should consist of (1) education on the disease process and pain mechanisms, posture, and work environment; (2) neck stretching and strengthening exercises; (3) massage over the cervical spine, particularly aimed at the muscle spasms; (4) joint manipulations over the cervical or thoracic spine; and potentially (5) TENS for pain control during activities and work. As discussed in Chapter 20, the mainstay of management for neck pain is advice encouraging return to usual activity and exercise. This approach is advocated in current clinical practice guidelines. Thus, initially, the focus of physical therapy treatment would start on education and self-management along with neck exercises. The approach could include booklets, websites, and videos, and can occur in individual or group session. The use of education alone is not effective, but when combined can provide improved adherence with an exercise program (Chapters 9 and 20). The types of exercise protocols range from ROM, strengthening, postural, motor control, and McKenzie exercises with no one exercise protocol being more effective than another. There is moderate evidence to support exercise in those with chronic neck pain (Chapter 20). As her primary complaint of neck pain resolves to a manageable level, the therapist would prescribe an aerobic exercise program on the basis of patient preference of activity. If the patient does not make significant improvements, remains unchanged, or gets worse within 1–2 weeks, then referral to a physician for more extensive screening is appropriate.

The addition of manual therapy techniques such as massage or joint mobilization would be initiated if the patient is not making satisfactory improvement. Evidence from systematic reviews suggests that manual therapy (massage and cervical manipulation) provides an improvement over no treatment or sham but is not superior to other treatments in either the short term or long term (Chapters 13 and 20). Additionally, thoracic manipulation may be an additional choice as there is an immediate effect in those with acute neck pain; however, effects for chronic neck pain are less clear (Chapter 13). Other electrophysical agents that could be added to facilitate recovery include TENS, low-level laser therapy, or traction. There is some evidence for traction in those with chronic neck pain (Chapter 20), TENS is effective for chronic

musculoskeletal pain but the evidence is unclear for neck pain (Chapters 11 and 20), and there is moderate evidence for use of low-level laser therapy (Chapters 12 and 20).

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