



Multimodal Analgesia for Chronic Pain

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Introduction

- The perception of pain depends upon neural signals that are processed at **multiple levels** from the periphery through the neuraxis to multiple areas within the cerebral cortex (Fig. 65.1, Chap. 1, chronic pain).
- Changes can occur at transcriptional, translational and posttranslational levels in both peripheral and central neurons. Peripheral neuronal sensitization is mainly mediated by inflammatory mediators whereas central sensitization results from repetitive discharges of C fibers (wind-up phenomenon, see Chap. 1, chronic pain).
- The descending pathways can modulate pain transmission via neurotransmitters including **endogenous opioids, serotonin, and norepinephrine**. Because of such complexities in the pathophysiology of chronic pain **multimodal treatment strategies** may be required (Fig. 65.1).
- Chronic pain is associated with disturbances in mood, sleep, energy, and daily activities which can affect the patient's mental, social, sexual, and general physical health (Chap. 3, chronic pain). In addition to pharmacologic therapy, chronic pain patients may benefit

from **education** about their condition and **psychotherapy** to improve coping skills and reduce anxiety, fear, and stress (Table 65.1).

- Multidisciplinary therapy can be offered in a gradual fashion as needed or in a formalized setting such as a structured **pain rehabilitation program**.

Multimodal Treatment Paradigms

1. Psychological comorbidities, if present, can be addressed with pain psychotherapy for mindfulness-based stress reduction, relaxation training, biofeedback, and CBT
2. Physical Therapy: graded exercise (land and aquatic), pacing, addressing fear avoidance and guarding
3. Mechanical treatments: Ice/heat, TENS, massage therapy
4. Integrated medicine: acupuncture, yoga, Tai Chi, chiropractic treatments
5. Lifestyle modification: Tobacco cessation, sleep hygiene, dietary counseling, weight loss
6. Interventional treatments: Steroid injections, nerve blocks, trigger point injections, neuromodulation
7. Multimodal medication therapies: Acetaminophen, NSAIDs, TCAs, SNRIs, muscle relaxants, topical medication, anti-convulsant

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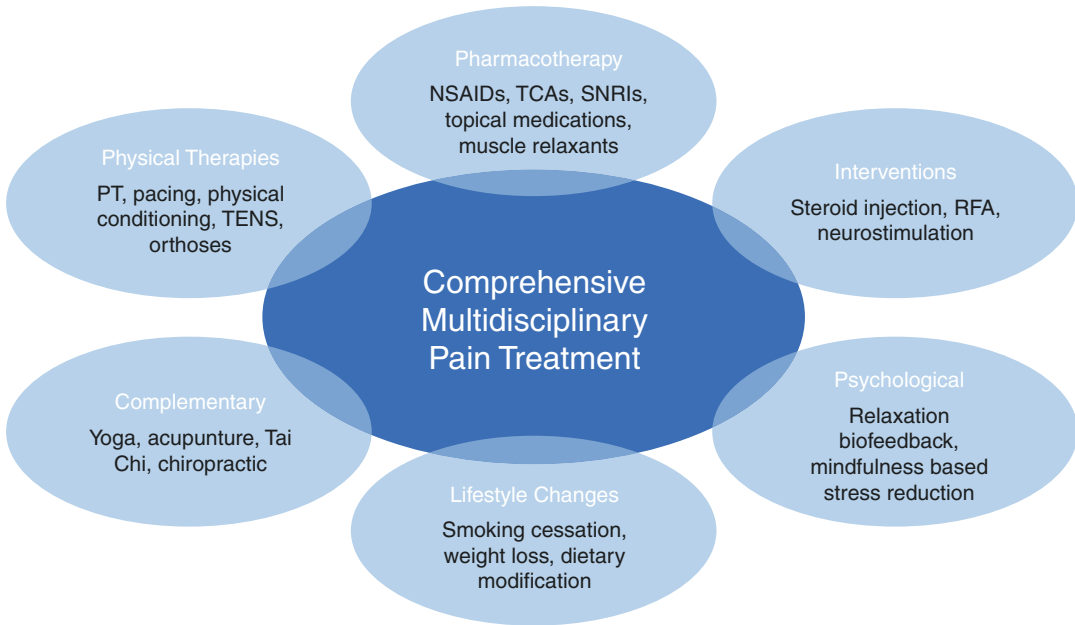


Fig. 65.1 Comprehensive multidisciplinary pain treatment. (Need to be drawn by a Springer illustrator)

Table 65.1 Behavioral interventions for chronic pain

Biofeedback	Patients are trained to influence physiologic processes—such as blood pressure, skin temperature—with the aid of visual or auditory devices that amplify these processes. Examples include electromyographic biofeedback, which measures tension in the frontalis muscle, and EEG biofeedback, which has been found effective in treating some chronic pain
CBT	Cognitive strategies and skills are taught so that maladaptive processes and irrational thinking, which directly affect perceptions and experiences, can be overcome
Hypnosis and guided imagery	With visualization and one’s imagination, patients can obtain a hypnotic state that is essentially aroused yet has little or no peripheral awareness. In guided imagery, patients focus on something (e.g., their chronic pain) that they would like to alter or eliminate. Suggestibility is an important element of both hypnosis and guided imagery
Meditation	In the health care setting, the forms of meditation that have been best researched include transcendental meditation and mindfulness meditation. In the former, the patient repeats a silent word or mantra to reduce and eventually transcend one’s internal dialogue. In the latter, the patient maintains a nonjudgmental state of awareness in which emotions, judgments, beliefs, and so on are addressed
Patient education	Teaching patients about common symptoms, possible adverse effects, appropriate treatments, self-care strategies, and the likely course of the discomfort has been found to reduce the anxiety that may be heightened in the uninformed, which in turn may prolong symptoms. Psychoeducational approaches broaden the scope of the training to include adaptive psychological strategies such as CBT
Relaxation techniques	Hypoarousal may be obtained from several relaxation procedures, the most studied of which is progressive muscle relaxation, which aims to reduce muscular tension by alternately tensing and relaxing muscles. Hypometabolic states in which sympathetic arousal is reduced—As in Benson’s relaxation response—Also may be achieved. These techniques can ameliorate symptoms that are associated with chronic pain, such as anxiety, fatigue, and sleep disturbance

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Drug Therapy

- Due to complex pathophysiology of chronic pain, a combination of medications is often required. Multimodal medication therapies are well established for the treatment of other diseases such as hypertension, diabetes, and depression [1, 2].
- The common classes of medication in the treatment of chronic pain include acetaminophen, NSAIDs, TCAs, SNRIs, muscle relaxants, topical medication, and anti-convulsants. Most analgesic and adjuvant drugs have sedative side effects and a ‘low and slow’ strategy (starting with low dose with slow upward titration) is suggested to balance effective treatment and acceptable side effects.
- Neuropathic pain (pain caused by nerve injury) such as spinal cord injury, multiple sclerosis, central post-stroke pain, diabetic neuropathy, postherpetic neuralgia, radiculopathy, and intercostal neuralgia are more likely to respond to gabapentoids, tricyclic antidepressant, and duloxetine (See Chap. 32, Chronic pain).
- Inflammatory pain (rheumatoid arthritis, osteoarthritis, etc.) pain typically responds to the combination of oral and topical NSAIDs (Chap. 31, chronic pain). Chronic low back pain has been shown to have both inflammatory and neuropathic component, which may require a combination of multiple medication classes to achieve optimal improvement.
- Management of patients with widespread pain will likely require multidisciplinary treatment including medications (NSAID medications, muscle relaxants, anti-neuropathic agents, and others), **group therapy, targeted physical therapy, social support, and pain psychotherapy** (Fig. 65.1).
- The prescription of opioids should be limited to **acute flare** of chronic pain conditions; starting with the lowest effective dose of immediate-release opioids (Table 33.3, Chap. 33, chronic pain) and at no greater quantity than needed for the expected duration of pain;

3 days or less often is sufficient; more than **7 days** is rarely needed.

Psychotherapy

- Cognitive Behavioral Therapy (CBT) with a **pain psychologist** may be beneficial for patients with comorbid anxiety, depression, PTSD, bipolar affective disorder, and others (Table 65.1).
- Additional evidence based pain psychology therapies include neurocognitive education, biofeedback, mindfulness based stress reduction, and relaxation strategies.
- Engagement in CBT and other pain psychology therapies is dependent on **patient motivation and engagement**, and benefit may be variable depending on the extent to which the patient is able or willing to engage with therapy
- In a population of patients with co-morbid pain and depression, those received treatment of depression (medications, therapies, or combination) were significantly less likely to report pain interference with work (OR 0.57) and a trend toward fewer limitations in their activities of daily living [5].
- The use of psychological modalities for the treatment of chronic pain predates many of our current interventional techniques, with the successful use of **operant conditioning** to achieve reductions in medication usage, improvements in self-reported pain, and improvements in physical function [6].
- For specific pain pathologies including phantom limb pain and complex regional pain syndrome, graded **motor imagery** has been shown to have long term benefit.

Physical Therapy

- Pain based physical therapy is guided by a physical therapist to provide therapeutic exercise, a home exercise program (HEP), and to

address **maladaptive pain behaviors** including fear avoidance and guarding.

- Therapeutic exercise involves physical movements, postures, or activities designed to ameliorate impairment, improve function, and enhance overall wellbeing of the patient. Manual stretching, myofascial therapy, dry needling, passive mobilization, and active exercises are also utilized.
- While the aggregate of studies evaluating the effectiveness of a wide range of physical activity and exercise programs across a myriad of painful conditions shows mixed value, there is little to no evidence of risk of harm [8].
- More focal studies evaluating the effect on low back pain have shown as much as 30% improvement in **Oswestry Disability Index** scores in as little as 4 weeks of treatment [9].

Orthoses or Prosthesis

- Patients with movement evoked pain or an antalgic gait may benefit from short term use of orthotics (braces, splints, etc.) to limit motions that incite pain. Long term use, however, is not recommended as the goal is to use PT to improve function.
- Appropriately fitted orthoses can also help treat and prevent the progression of **phantom limb** and residual limb pain.

Mechanical Modalities

- The application of heat or cold, and TENS unit to localized area of pain can provide short term pain relief. These modalities are particularly useful when pain is mild or moderate.
- Transcutaneous electrical nerve stimulation (TENS) is a widely available modality for the treatment of myofascial and superficial neuropathic pain. TENS can be tried as a supervised trial when working with a physical therapist.
- Cold application with cold packs and/or menthol based topical products may reduce myofascial pain. Possible mechanism include initial vasoconstriction, followed by vasodila-

tion, however patients should be advised about the risks of prolonged or excessive exposure.

- Heat application increases blood flow and has soothing effect. Superficial heating with hot packs, heating pads, or baths can improve chronic pain in the joints and muscles, however like with cold application, patients should be advised about the risks of prolonged exposure.

Interventions

- Injections of local anesthetic and/or steroid medication are intended to provide **temporary pain relief** by stopping the pain cycle. One of the most common pain injections is an epidural steroid injection (Chap. 10, chronic pain) and other common procedures include facet joint injections, selective nerve root blocks, sacroiliac joint injections, and peripheral nerve blocks.
- Some injections are primarily for diagnostic purposes and can be used to isolate pain generating structures for further intervention such as **radiofrequency ablation** or surgery.
- Although most pain procedures are short lasting with pain relief pain for 1 to 12 months, they enable patients to be **engaged in physical therapy** and help in addressing underlying physical problems causing pain.
- Intrathecal pain pump or spinal cord stimulation may offer long lasting pain relief in select patients (Chap. 27, chronic pain).
- Although interventional procedures have an excellent safety profile, they are **rarely indicated** as stand alone first-line treatments.

Complementary and Alternative Medicine

The complementary and alternative medicine strategies such as acupuncture, yoga, massage therapy, and Tai-chi have been widely used, but there is not enough high-quality research to make a recommendation to include them in the multimodal integrative therapies for chronic pain. In

most cases, the risks associated with these treatments are **low** and they can be included in a multidisciplinary treatment program if patients **express interest in them**.

Emerging Modalities

- **Transcranial Magnetic Stimulation (TMS):** The application of an electromagnetic field exterior to the skull which produces changes in cell signaling in targeted areas of the brain. The treatment is currently being evaluated for efficacy in chronic pain, depression, PTSD, and other conditions [10].
- **Platelet Rich Plasma (PRP):** Isolated plasma concentrates of a patient's own blood containing growth factors to stimulate tissues **regeneration**. These are commonly injected into joints to facilitate enhanced recovery of tissues with low baseline perfusion (eg. Tendinitis) [11].
- **Stem cell therapies:** The basis of this therapy is to inject undifferentiated cells to promote the repair response of diseased, dysfunctional, or damaged tissues. In addition, stem cells release neurotrophic factors, which helps in replacing the injured neural cells, making them good candidates for neuropathic pain. However, the use of stem cells is still in the early stages due to various ethical problems.

Clinical Pearls

- In summary, the optimal treatment of chronic pain will often require the employment of multiple domains of treatment including **interventional, pharmacologic, physical, and psychological**.
- It is also important to remember that greater progress can be achieved in the treatment of patients with chronic pain when multiple domains of life, including pain severity, physical function, well-being, and mental wellness are used to assess progress.

- While the moonshot goal of the elimination of pain should never be abandoned, seeking improvements across multiple domains of the patient's pain experience will help to improve overall patient satisfaction, adherence, and outcomes [7].

Questions

1. A 30 year old male diagnosed with post amputation pain 6 weeks after a left BKA should be treated with all of the following as initial therapy **EXCEPT**:
 - A. Opioids
 - B. Tricyclic antidepressant medications
 - C. Physical therapy and orthotics
 - D. Graded motor imagery
2. A 56 year old male is POD 3 from spine surgery. He reports incomplete analgesia with 10 mg of oxycodone Q4 hours. Which medication change is most appropriate?
 - A. Increase oxycodone to 20 mg Q4 hours
 - B. Initiate IV ketamine infusion
 - C. Restart patient controlled analgesia (PCA) with morphine
 - D. Start Acetaminophen 1000 mg Q8h
3. Which of the following side effects is **least** likely to occur in association with increases in opioid medications?
 - A. Diarrhea
 - B. Respiratory depression
 - C. Pruritis
 - D. Sedation
4. A 35 year old female presents to her PCP with new onset low back pain that occurred while exercising. Neurological examination is unremarkable and physical examination only reveals lumbar paraspinal tenderness. Which of the following is an appropriate initial recommendation?
 - A. Lumbar MRI
 - B. Referral for lumbar epidural steroid
 - C. NSAID medications and physical therapy referral
 - D. All of the above

Answers

1. A: Tricyclic Antidepressant medications, graded motor imagery, physical therapy, and orthotic use have all been shown to provide relief at by various mechanisms of action for patients with post amputation pain. Opioid medications are not contraindicated, but are not considered first line therapy outside of the immediate post-operative period.
2. D: The addition of non-opioid medication to an opioid regimen is more likely to produce improvements in analgesia than an increase in opioid medication [3, 4]. IV ketamine infusion and opioid PCA are appropriate therapies for poorly controlled pain, however this should be limited to the post-operative period, and should be only be initiated after the initiation of a multimodal medication regimen.
3. A: Constipation is a common side effect from opioid medications, as are the remaining choices.
4. C: In the absence of neurological findings or radicular pain, the initial treatment for mechanical low back pain in low risk individuals is includes non-opioid analgesics and physical therapy. If the pain fails to resolve, is accompanied by radicular pain or neurologic findings, or is accompanied by other constitutional symptoms such as weight loss or fever, additional work up and/or procedures may be indicated.

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