Chapter

Conceptualizing Drug Addiction and Chronic Pain through a Biopsychosocial Framework to Improve Therapeutic Strategies

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Abstract

The recent surge in opioid-related deaths has brought poor pain management practices to the forefront of our nation's collective consciousness. However, improving treatments for chronic pain, substance use disorders (SUD), and comorbid expression of both requires a better understanding of the pathophysiology involved in their development. In this chapter, the authors present the argument that chronic pain and SUD can be conceptualized similarly from a biopsychosocial perspective to inform a better approach to treatment. The authors describe the common neurobehavioral mechanisms of SUD and chronic pain, then discuss the efficacy of several psychotherapeutic methods employed to combat chronic pain, addiction, and related disorders. Such methods may contribute to positive health outcomes in managing chronic pain and curbing drug addiction by reducing the role of opioid analgesics for long-term pain management.

Keywords: addiction, substance use disorders, chronic pain, opioids, psychotherapy, cognitive behavioral therapy, mindfulness-based stress reduction, solution-focused brief psychotherapy, motivational interviewing

1. Introduction

Over the past two decades, the rate of prescription drug misuse has been rapidly increasing worldwide, leading to a growing number of emergency department visits, hospitalizations, and overdose deaths. The National Safety Council reported that in 2017, it was more common to die of opioid overdose than in a car crash, and by 2018, drug overdose became the number 1 cause of unintentional death in the United States. The coronavirus pandemic has only exacerbated this situation [1]. Opioid analgesics have become the most commonly prescribed class of drugs in the United States [2] in part because approximately 100 million American adults suffer from chronic pain, more than those affected by heart disease, diabetes, and cancer combined [3]. The other major piece of this puzzle is that prescription opioids were misrepresented by pharmaceutical manufacturers as non-addictive, which led to widespread over-prescription of opioids for long-term chronic pain management. Although the addictive potential of oxycodone was recognized very early [4], very few studies have been conducted on this or other opioid painkillers. Recently, the

growing recognition that prescription opioids can be addictive has also led some doctors to over-correct the problem by not prescribing sufficient opioids to manage pain when it is appropriate, leaving patients to seek illegal sources or substances (e.g. heroin) to manage pain and physical withdrawal symptoms. These opposing but equally ill-informed prescription practices have culminated into a single outcome: an epidemic of opioid addiction and death in the United States.

From many different perspectives, chronic pain and substance use disorders (SUD) share a plethora of similarities and thus it is not surprising that they frequently occur in tandem, with either one preceding the other. Overall, the prevalence of chronic pain in individuals with SUD is estimated to be 27–87%, with individuals suffering from chronic pain 2-3X more likely to experience a SUD, and individuals that have a SUD 1.5 times more likely to experience chronic pain [5]. In people receiving an opioid prescription for long-term chronic pain treatment, 21–29% misuse the opioid medication and 8–12% develop an opioid use disorder (OUD) [6, 7], though some estimates are as high as 43%, with elevated risk for other substance-related disorders as well [5]. Some hypothesize that individuals self-medicate with drugs to manage the psychological aspects of pain [8, 9], while others suggest pre-existing physiological and psychological characteristics associated with OUD/SUD can be stimulated by a chronic pain condition [9, 10]. These hypotheses are not mutually exclusive, and draw attention to the fact that the relationship between chronic pain and SUD is difficult to disentangle, making it complicated to establish effective treatments.

As with many societal weaknesses exposed by the pandemic, SUD, particularly OUD, are flourishing and overdose deaths continue to rise [1]. This does not appear to be due solely to the disease itself, but rather the significant increase in life stress (e.g. job loss, social isolation, etc.) combined with lack of access to proper mental and physical health care. This illustrates well the central hypothesis we aim to present: that a biopsychosocial perspective of addiction and chronic pain, which incorporates factors from the societal to molecular levels, allows for a more thorough understanding of these disorders. We suggest that incorporating alternative therapeutic methods and reducing the role of opioid analgesics for long-term pain management may contribute to positive health outcomes in managing chronic pain, addiction, and comorbid expression of both.

2. Biopsychosocial approach to understanding health and disease

As the name suggests, the biopsychosocial (BPS) model proposes that healthcare professionals use biological, psychological, behavioral, and social lenses to understand health and disease. Psychiatrist George Engel has been credited with the formulation, and call for action, that propelled the understanding of disease and illness past that of basic Renaissance philosophy and into an understanding not solely based in biological factors [11]. Engel introduced the BPS model as a contrast to the biomedical model of health and disease, which had long reigned supreme (and still predominates clinical practice in many fields). His model also contrasts with a purely environmental/ecological model, which holds a more holistic view of health, but may neglect the importance of biological influences. The BPS model incorporates the best of both worlds, recognizing that both nature and nurture are vitally important to health and disease. This new ideal formed the foundation for behavioral and psychological conceptualizations of health and medicine [12].

The BPS model has now become the leading one in conceptualizing many forms of illness, including chronic pain, although it continues to be underutilized in practice, particularly in acute medical and surgical fields of study that prioritize biomedical

views of disease and illness [13]. A large part of the problem in translating concept to practice is that the BPS model has minimal influence over provisional healthcare funding [13]. Critics of the BPS model claim that the diagnostic front would be marginalized by utilizing a threefold framework (although this had already been addressed by functional and practical analysis) [14, 15]. Biomedical model proponents suggest that the BPS model may promote a lack of focus, or that practitioners may misjudge other significant factors related to treatment, and therefore cause unintended harm to patients due to the complexity of the biopsychosocial approach and the negligence that may occur [14]. However, it is important to consider that harm can be associated with any models or frameworks, and that harm primarily results from misuse of models and failures to recognize limitations of those models [13].

The opioid epidemic is a profound and tragic illustration of the problems associated with the persistence of the biomedical model in many fields and countries (including the U.S.). This model has seen healthcare costs soar, while patient outcomes have fallen. A major cause of these failings is the lack of consideration of psychosocial factors in patients' lives, which can contribute greatly to overall health. Two recent Nature articles have drawn attention to the importance of social context - and the shortcomings of a biomedical-only approach - in relation to substance use. Hart (2017) argues that even conceptualizing addiction as a disease or disorder is not only inaccurate, but harmful, contributing to social injustice in the form of racism and socioeconomic marginalization [16]. He further takes issue with the exaggerated value placed upon neuroscientific evidence. Relatedly, Heilig et al. (2016) attributes the relative lack of addiction treatment advancements to the glaring omission of social context in neuroscience, and calls on the field to elucidate the impacts of social exclusion and marginalization on the development of drug-seeking and consumption [17]. Although these articles focus on addiction, the principles apply to chronic pain as well.

While solving the socioeconomic disparities that contribute to illness will be a formidable task that lies outside the scope of the current chapter, the authors argue that a biopsychosocial approach to addiction and chronic pain is superior to a strictly biomedical one, and that it has the potential to counteract the problems of a biomedical-only view. As noted above, the biomedical paradigm is struggling to confront rising healthcare costs and poor, patient-reported outcomes [13]. The BPS model, prided on person-centered care, can alleviate this financial and diagnostic burden, particularly as it relates to chronic pain, mental illness, and other functional disorders [13, 18]. The BPS model has the ability to yield more positive patient-reported outcomes of treatment, especially within the context of cognitive behavioral therapy, due to the person-centered approach and use of goal-setting, which has recognized utility in treating both chronic pain and SUD [19–21]. Family involvement in treatment can heavily reduce stigma related to SUD and chronic pain, and this social engagement is correlated with lasting, positive treatment outcomes [22]. If this model becomes more ingrained within the cultural sphere of Western clinical medicine and the general populace, it is predicted to drastically reduce societal stigma related to both chronic pain and SUD, thus altering perceived treatment outcomes and making non-pharmacological treatment more acceptable and accessible to those suffering [23]. Considerations of the social aspects of the BPS model would greatly advance future research, particularly that relating to psychological and behavioral functioning.

3. Neurobiological overlap between addiction and chronic pain

Epidemiological and functional imaging studies suggest a bidirectional relationship between chronic pain and many psychiatric disorders, including SUD, and that

significant neurological overlap exists between them [5, 24, 25]. As described below, these similarities in affect, cognition, and behavior between addiction and chronic pain are reflected by similar changes in neural circuitry. These conditions also share many genetic and epigenetic mechanisms, but a detailed discussion is outside the focus of this chapter.

3.1 Neurobiology of substance use disorders

SUD are undeniably biopsychosocial in nature and expression, with hallmark features of impaired daily functioning in cognitive, physiological, psychological, and social domains as a result of substance use and continued use despite these negative consequences. Diagnostic criteria for SUD include impaired cognitive and behavioral control over drug use, social impairment, such as job or relationship loss, use of drugs in risky or inappropriate situations that pose physical or psychological harm, and pharmacological criteria such as tolerance and withdrawal [26]. Neuroscientists conceptualize the addicted brain in a framework that encompasses key elements of two theories of motivated behavior: incentive-sensitization theory, wherein the motivation to consume drugs is said to result from conditioned reinforcement and over-attribution of salience to drugs and drug cues [27], and opponent-processes theory [28], which holds that the motivation to consume drugs is initially driven by positive reinforcement (addition of pleasurable feelings or euphoria, e.g. reward/process A), but repeated drug use is driven by negative reinforcement (subtraction of aversive feelings or state associated with drug deprivation, e.g. antireward/process B). These theories have given rise to the concept of the addiction cycle, which is supported by abundant neuroscientific evidence (reviewed extensively in [29] and summarized below).

The addiction cycle is composed of three stages, each underlain by neuroplastic changes in the function of discrete brain circuits resulting from chronic drug exposure, with variability modulated by an individual's genetics, life experiences, and their drug(s) of choice. The binge/intoxication stage is characterized by drug-induced positive reinforcement and loss of control over the amount and duration of drug-taking. The main circuit involved in acute drug reinforcement is the dopaminergic projection from the ventral tegmental area (VTA) to the nucleus accumbens (NAc), supported by the central nucleus of the amygdala (CeA) and ventral pallidum (VP), while compulsivity in drug-taking involves the caudate/putamen (CPu). Repeated drug use reduces baseline activity of these circuits, partly setting the stage for withdrawal/negative affect to drive drug-taking. The withdrawal/negative affect stage is marked by negative reinforcement (removal of unpleasant stimulus or emotional state) driven by the recruitment of the hypothalamic–pituitary–adrenal (HPA) stress axis and circuitry connecting the basolateral amygdala (BLA) and hippocampus to the extended amygdala, CeA, basal nucleus of the stria terminalis (BNST), and a subregion of the NAc shell, which in turn project to the VP and lateral hypothalamus (LH). Acute withdrawal from several drugs, including opioids, involves hyperactive corticotropin-releasing factor (CRF) and norepinephrine (NE) neurotransmitter systems, the endogenous antireward opioid dynorphin, substance P, neuropeptide Y, vasopressin, and nociceptin. The preoccupation/anticipation stage is marked by drug craving, key to the relapsing nature of the addiction cycle. The impetus of relapse determines the neurocircuitry involved, with drug-induced relapse regulated by glutamatergic projections from the medial PFC (mPFC) to the NAc and VP, cue-induced relapse regulated by BLA-PFC-NAc glutamate signaling and VTA-PFC dopamine signaling, and stress-induced relapse activating the extended amygdalar CRF and NE systems. Compromised cognition, memory, and inhibitory control involve the

hippocampus, mPFC and orbitofrontal cortex (OFC; [29]. As the authors discuss below, many of the structures, circuits, and neurochemical mediators that drive SUD are also involved in chronic pain.

3.2 Neurobiology of chronic pain

Nociception is a physiological response to a noxious stimulus wherein normally silent sensory neurons called nociceptors deliver information to the brain to elicit protective actions [30]. When stimulated, nociceptors transduce signals along spinal cord primary afferent Aδ and C fibers and converge at the dorsal horn, where afferent neurons in laminae I and V provide input to the brain [31]. Pain results from the activation of a distributed group of brain structures within the brainstem reticular formation and the limbic system, collectively referred to as the pain neuromatrix [32], a three-tiered hierarchy of experiential pain processing [33]. First order processing occurs when the spinothalamic and spinoreticulothalamic tracts carry signals from the dorsal horn into the brainstem and posterior thalamus (pTHAL), which encodes localization of pain and identification of specialized pain characteristics [31, 33]. The second tier involves perceptive and attentional internalization of pain, including cognitive structuring and modulation, attenuation, and proposition of somatic reactions to the painful stimuli, and is regulated by the posterior parietal cortex (pPAR), anterior cingulate cortex (ACC), PFC, and insula [33]. The third tier is characterized by emotional reappraisal of the nociceptive stimuli, in which emotional context is applied to the experience to modulate its psychological and social consequences. The brain regions associated with this tier are the pPAR, OFC, and anterolateral PFC [33]. These cortical structures are responsible for determining the behavioral response to nociceptive stimulation [31, 34].

Chronic pain is defined as persisting past the normal time of healing, generally for six months or more [35]. Unlike acute pain, which is protective in nature, chronic pain has negative effects on psychological and social well-being. As with SUD, chronic pain is the result of the plastic nature of molecules and circuits within the nervous system [31]. When activated persistently, the pain neuromatrix and other regions of the brain and spinal cord involved in nociceptive and cognitive-evaluative processing undergo neuroplastic changes that amplify activity, called central sensitization [36–38]. These changes result in exaggerated responses to noxious stimuli (hyperalgesia) and pain responses being triggered by normally innocuous stimuli (allodynia). The transition from acute to chronic pain is underlain by greater engagement of emotional and motivational circuitry [39], paralleling the progression through the addiction cycle.

Not surprisingly, research suggests that there is significant overlap in the neurological mechanisms involved in chronic pain with those involved in drug addiction [29, 40, 41]. Neuroplastic changes in corticolimbic structures comparable to those seen in SUD also contribute to pain chronification [42]. Specifically, chronic pain, like SUD, involves neuroadaptations that dampen reward, recruit stress-related circuitry, and promote aberrant learning that converge to negatively affect physiology and behavior [39, 42–45]. Chronic pain can disrupt the reward/antireward balance through persistent sensitization of nociceptive circuitry within the NAc, and attenuation of behavioral inhibitory signaling from the habenula [46, 47] to produce an overall shift in reward level or hedonic tone [48]. NAc functional connectivity changes have also been associated with risk-taking behavior in chronic pain patients, with high gain sensitivity in sufferers of chronic back pain correlated to greater connectivity between NAc and subcortical areas, compared to controls with strong NAc-frontal cortex connectivity [49]. These changes can promote the use of alcohol and drugs, particularly opioids, for negative reinforcement

(alleviating physical and psychological pain) and ultimately predispose chronic pain sufferers to develop drug addiction [39, 43].

As discussed above, both repeated exposure to addictive drugs and chronic pain lead to changes in brain function that promote continued drug use. Conversely, recurring drug use can also promote the development of chronic pain, illustrating the logical fallacy in treating chronic pain with prescription opioids. As with other addictive drugs, repeated opioid administration can shift the balance between reward and antireward processes, affecting the ability to experience positive emotions from natural rewards over time [47]. This shift in balance is accompanied by amplification of the antireward state, effectively establishing a reward deficit state, which drives further opioid use to compensate [47, 50]. Allostatic changes from pain stimuli are amplified when opioids are misused [51–53], resulting in neural adaptations that promote hyperalgesia, drug tolerance, and difficulty regulating emotion, which can in turn amplify anhedonia, producing a downward spiral of chronic pain and further prescription opioid misuse [53].

4. Shared psychosocial factors in addiction and chronic pain

As is evident from the sections above summarizing neural circuitry involved in addiction and chronic pain, the boundary between the neurobiological and psychological aspects of these conditions is somewhat arbitrary. Likewise, the boundary between the psychological and social components is poorly defined, reflecting the central concept of the BPS model, that health and disease involve biological, psychological, and social factors that influence one another in a reciprocal, highly dynamic manner [54]. Meints and Edwards (2018) divide psychosocial variables involved in chronic pain into two main categories. General psychosocial factors include affect, trauma, social/interpersonal disposition, sex- and race-related disparities, and pain-specific psychosocial factors include catastrophizing, coping, expectations, and self-efficacy [54]. Another way of conceptualizing the division is factors that predispose an individual to develop chronic pain and those that emerge as a consequence of pain. As discussed below, there is a high degree of overlap between the psychosocial aspects of chronic pain and addiction, and it is not always easy to make the distinction between cause and consequence in SUD.

Psychosocial factors influencing reward, stress, and motivation can contribute to a downward spiral of chronic pain and comorbid conditions [46]. It is well-known that negative affect promotes drug use, while conversely, repeated drug use increases risk for depression and anxiety. Similarly, anhedonic depressive symptoms often exceed 50% comorbidity in individuals suffering from fibromyalgia, temporomandibular joint disorder, chronic spinal pain, and chronic abdominal pain [5]. Symptoms of depression and anxiety are prominent in both episodic and chronic cluster headaches, with those in the chronic subset being less likely to cognitively reframe their pain sensations and more likely to ruminate [55]. In contrast to the bidirectional nature of negative affect and SUD, depression and anxiety are strong predictors of pain and related disability, but neither pain nor related disability appear to be good predictors of depression and anxiety [54]. Affective factors are a strong predictors of opioid misuse, with mood disorders, anxiety disorders, and chronic pain conditions either preceding or overlapping with OUD [9, 56–60]. Furthermore, negative affect and cognitions increase risk of developing an OUD in surgical patients, as their pre-operative presence were major predictors of prolonged opioid cessation following the operation [61]. Childhood physical, psychological, and sexual abuse have been implicated in later-life development of several chronic pain conditions [54], as well as alcohol and drug abuse [62]. Post-traumatic

stress disorder (PTSD) in adult veterans (which can be related to combat exposure and/or injuries such as traumatic brain injury) and in victims of childhood abuse are highly associated with development of chronic pain [54] and substance use [63].

Deficits in executive function can contribute to and result from repeated drug use. Likewise, chronic pain is associated with impairments in memory, attention, and cognitive flexibility, although the relationship is a complex one, owing to a lack of standard tests and poor control of confounding variables such as sleep and medication in existing studies [64]. Working memory and emotional control were shown to be impaired in chronic pain patients, but neither the intensity nor the duration of pain itself predicted executive dysfunction [65]. As with negative affect, poor executive function may predispose the development of chronic pain, a notion supported by a recent study wherein poor cognitive performance before surgery on Trail-Making Test B and Rey-Osterrieth Complex Figure copy and recall predicted the persistence of pain up to 12 months after surgery [66]. Relatedly, while impulsivity is not generally prominent in chronic pain patients [67], this trait is quite pronounced in SUD [29] and may play a key role in determining the likelihood of opioid misuse in pain patients. Specifically, urgency and attentional impulsivity have been implicated in current and future misuse of opioids by chronic pain patients, while sensation-seeking seems to have little to no influence [67, 68]. High baseline impulsivity in rats was also correlated with high impulsivity in the variable delay-to-signal test after spared nerve injury [69]. Additionally, a recent study showed that decision-making in the Iowa Gambling Task by chronic pain patients was robustly modeled mathematically by over-valuation of gains and under-valuation of losses, typical of risk-taking [70]. Risky decision-making and lifestyle is also highly prevalent with long-term substance use [9], which may, in turn, increase risk for developing a chronic pain condition. For example, prescription opioid use was associated with a 47% increased risk of car crash initiation, and thus, injury [6]. Other drug-associated behavior, such as injecting and high-risk or illegal activity to obtain drugs could also contribute to chronic pain and vice versa.

Much research underscores the importance of social support in ameliorating pain and improving function in chronic pain [12, 54], as well as preventing relapse in SUD [71]. However, negative social interactions can have the opposite effect. For example, the "sick role" of individuals experiencing chronic pain is a social context accompanied by attention, pity, and permitted exemption from daily routines [40]. Although moderately pleasurable for the individual experiencing pain, socio-emotional pain relief is stressful for family and friends, and may promote aversion and distaste of the individual that has assumed it. This can cause isolation, communication deficits, emotional setbacks, and may amplify the original chronic pain state without the presence of a nociceptive stimulus [72]. Similarly, psychosocial stressors such as aversion, isolation, and other emotional setbacks are also heavily apparent in addiction and other mood disorders [8, 10]. Relatedly, family members and peers attitudes and behaviors also influence individuals with chronic pain and SUD. Parental catastrophizing, spousal/partner depression or avoidant, anxious attachment styles, lack of social support at work, and negative interactions with co-workers and workmans compensation programs can all promote chronic pain and disability [54]. Similar interpersonal factors are at play with SUD [73], and they can be particularly important for adolescents, whose peers and parents exert heavy influences over substance use by affecting availability of drugs and the child's perception of approval/disapproval of drug use [74]. Therapies targeting positive behavioral change in the social context may be essential in combating both chronic pain and SUD.

In addition to interpersonal factors, gender and race are other aspects of the social milieu that can have profound positive or negative effects on physical and

mental health. While there can clearly be biological influences in both cases, such as chromosomal and hormonal influences in gender, and genetic variability in race, it is worth considering the social features, which may be even more important in determining risk for mental health-related functioning (as appears to be the case for schizophrenia; [75]). Females have a higher prevalence of pain, decreased pain threshold, more severe, recurrent, and longer duration of pain compared to males, differences explained at least in part by social factors, such as gender roles and differences in coping strategies [54]. Compared to men, women also show greater propensity for addiction to many drugs, including opioids, but research seems to have focused primarily on potential biological explanations for such differences [76, 77]. The negative impacts of alcohol and drug use are greater on Black and Hispanic Americans, although consumption patterns between Blacks, Hispanics, and Whites do not explain this difference (at least in relation to alcohol; [78]). Data are lacking for many ethnic groups regarding chronic pain, but Blacks and Asian Americans report higher levels of pain and lower pain tolerance compared to Caucasians, differences which may stem from racism, socioeconomic strain, and ineffective pain coping strategies [54]. Other structural vulnerability factors such as poor access to health care are likely to contribute to the unequal impacts of SUD and chronic pain on minority groups [79]. Further research is needed to gain a better understanding of how complex social and structural factors shape risk for chronic pain and SUD. The field of epigenetics, which has begun to address the neurobiological effects of well-known social context-related risk factors for schizophrenia - early life adversity, growing up in an urban environment, minority group position, and cannabis use [75] - holds great promise in advancing science, therapeutics, and social change, and underscores the strengths of the biopsychosocial perspective.

5. Non-pharmacological treatments for addiction and chronic pain

The focus of biomedical interventions to manage chronic pain is primarily pharmacological, using opioid analgesics or surgical procedures [80]. However, surgery inherently subjects patients to risks associated with the surgical procedures, including more pain [80]. Likewise, opioids do not show substantial evidence for beneficial long-term pain management [80–82] and as discussed above, may even exacerbate it. For example, in a study of 26,014 individuals experiencing chronic back pain, psychological distress (depression, anxiety, posttraumatic stress disorder, and SUD), unhealthy lifestyle (obesity and smoking), and health care utilization increased incrementally with duration of opioid use [83]. As chronic pain and long-term opioid use may cross-sensitize across multiple biopsychosocial domains, it is essential to identify alternative treatment options.

A large body of clinical evidence suggests that treatments such as cognitive behavioral therapy (CBT) and mindfulness-based stress reduction (MBSR) alleviate symptoms of depression, anxiety, SUD, and chronic pain [84] and that the core mesocorticolimbic structures impacted by SUD and chronic pain can be effectively targeted by innovative therapies [85]. The CDC has also recommended treatments like exercise therapy and CBT to reduce pain and improve function in patients with chronic pain [86]. These alternative treatments aim to directly dismantle the negative biofeedback created by drug- or pain-induced maladaptive changes within reward and stress circuitry. Although more research is needed, the authors suggest that a more integrated approach for managing chronic pain and addiction should include clinical mental health therapeutic techniques, discussed below.

5.1 Cognitive behavioral therapy (CBT)

The goal of cognitive behavioral therapy (CBT) is to educate the client in the realm of positive coping strategies utilizing cognitive, respondent, and behavioral techniques [87]. CBT is designed to manage individual patient characteristics through a collaborative reframing of negative prediction, selective abstraction, and depersonalization to help the patient assume responsibility for their cognitions and behaviors. Cognitive behavioral therapists highlight the direct link between negative emotional states, sedentary cognitions, and resulting behaviors and seek to alter them in a holistic fashion that allows patients to grow through therapeutic change. This patient-therapist collaboration shakes sedentary perspectives and faulty core beliefs surrounding their ailment and allows the patient to reframe their thoughts and learn from new experiences.

Many individuals with SUD present to treatment unwillingly and approximately 45–50% will continue to use one or more drugs while in treatment [88]. In one study, CBT-treated individuals with SUD showed a 31% rate of abstinence compared to 13% abstinence rate in controls [89]. Compared to other psychosocial treatments, such as insight-oriented therapies involving psychoeducation, CBT appears more durable [90]. In the context of OUD, studies have shown that CBT alone does not lead to consistent therapeutic outcomes in patients, although it does seem to enhance the effects of methadone maintenance treatments (MMT) [91–93]. Combined treatment outcomes include greater attendance and treatment adherence and an increase in abstinence as evidenced by urine toxicology [88, 94]. Although reductions in substance use are often modest, sleeper effects, the notion that positive responses to CBT will increase over time, have been historically documented [95]. Relatedly, compared to MMT-only groups, or MMT and another independent counseling strategy, CBT has been associated with latent positive effects on psychosocial functioning. For example, employment consistency was shown to increase in parallel to daily functioning, and stress was shown to decrease with increased cognitive coping skills, reduced opioid use, and less depressive symptomology [91, 92]. Contingency management utilized within the context of CBT has been found to increase the likelihood of abstinence, and therefore may further enhance effectiveness of SUD treatment [89, 96]. A study in rats also supports the use of contingency management to enhance the relative value of nondrug reinforcers (in this case, delayed food reward) versus immediate opioid delivery, suggesting that people may similarly develop delay-discounting (a behavioral component of impulsivity) because of contingencies in their environment [97]. Combining pharmacological treatment with CBT to increase coping skills appears to be a promising strategy for SUD and its effectiveness may lie in addressing the individual's biopsychosocial functioning rather than simply treating withdrawal symptoms.

Recent international guidelines prescribe psychological interventions, rather than strictly pharmacological interventions, for the treatment of chronic nociceptive pain [98]. In chronic pain, CBT aims to help the patient channel their pain-related negative affect pain into a new cognitive interpretation of their sensations to increase their quality of life. Evidence has shown that outcomes from CBT-based interventions for chronic pain are moderate and comparable in efficacy to those for SUD. While CBT does not have a direct impact on the disability causing chronic pain [99], it has positive effects on patients' cognitions and appears to increase quality of life. For example, participants were 3X as likely to report no pain interference after CBT techniques to target and reframe negative cognitive patterns associated with the perceptions of pain [100]. Likewise, unrelenting chronic pain from terminal illness can increase desire for hastened death, but CBT-based activities like education, targeting of negative appraisal states, and relaxation association have been shown

to allow management and attenuation of pain [101]. Experimental, graded *in vivo* exposure therapy, a broad-spectrum CBT technique, has been shown to have some success in targeting the fear-avoidance model of chronic pain. Here, exposure to fearful movements gradually reduces classically conditioned fear/anxiety to reduce avoidance of these movements over the long-term [102]. Although more research is necessary, CBT appears promising as an adjunctive treatment in chronic pain. It may also be effective in augmenting treatment for patients with comorbid chronic pain and OUD by targeting patients' ability to cope with pain- and stress-related opioid craving.

5.2 Mindfulness-based stress reduction (MBSR)

Mindfulness is a novel treatment strategy with roots in Eastern religions and philosophies that aims to enhance the experience and understanding of positive emotions and dismantle aberrant learning underlying pathological thoughts and behaviors. At the core of mindful therapeutic practice is acceptance that the stressors that trigger drug use or exacerbate chronic pain cannot be eliminated from one's life, but that their responses to those stressors can be modified. Relatedly, MBSR teaches a non-judgmental approach to affective, cognitive, and behavioral states; whether a particular stimulus is positive or aversive makes no difference. Invocation of the present moment is also key, allowing the patient to moderate their awareness and attention by attending to themselves in the here-and-now. The idea is that this systematic awareness of the present state coupled with a non-judgmental, accepting attitude ameliorates stress by weakening the negative emotional states attached to stressors, and thereby interrupting the cycle of addiction/chronic pain and eliminating the need to self-medicate.

Mindfulness programs are particularly efficacious for SUD because they address aberrant learning related to distressing stimuli and promote an openness to experience that leads to a reduction in future distress from those stimuli [103], rather than promoting avoidance of stressors or triggers, which does not address the underlying pathology. Mindfulness strategies also lead to pro-adaptive changes in intrapersonal thought patterns and ingrained belief systems, such as cues and cravings [104], while momentary awareness enhances an individual's ability to accept and cope with negative experiences, such as relapse and risky behavior [105]. This momentary acceptance of unpleasant stimuli leads to neurobiological alterations related to new learning, and consequently protects against relapse [103]. MBSR has been found to alter neurostructural changes in the mesocorticolimbic system and reduce autonomic arousal, physiological correlates to individual perceptual shifts, value and priority clarification, increased self-awareness, urge and craving shifts, and the ability to "let go" [106]. This sensory- and perception-focused strategy system has also been found to positively impact hedonic processing in the context of chronic pain and opioid management that interferes with habit-forming behaviors associated with addiction [107].

MBSR and similar strategies that target aberrant learning have been shown to interrupt the progression of addiction to opioids [107]. Mindfulness trainings reduce the intense neural reactivity to drug-cues, reduce cravings, and uncouple negative affective states from the previously induced, self-medicated state [108]. Functional MRI studies have revealed that MBSR can enhance top-down limbic-striatal connections by strengthening associations between the PFC and the parietal regions of the brain [109, 110], suppressing the influences of craving and autonomic responses, and enhancing cognitive control and flexibility related to attention [109]. Furthermore, by promoting gratitude for positive experiences and acceptance of negative physical and affective states, MBSR has been shown to

reduce craving, downregulate sympathetic arousal, and heighten natural reward [111], essentially breaking the cycle of addiction. Compared to typical treatments for OUD that focus patient attention on suppression of craving, which can actually increase self-medication and relapse, mindfulness strategies that focus the attention of the patient on acceptance of substance use uncouples opioid craving and opioid use to promote long-term relapse prevention [109, 112, 113].

Utilizing mindfulness in the context of treating chronic pain is new to Western society. Eastern practices, such as Zen Buddhism and Hatha yoga, have been applied to a plethora of physical ailments for centuries, but now these are combined with traditional psychotherapies such as CBT and acceptance and commitment therapy [114]. As in addiction treatment, a non-judgmental stance is vitally important to MBSR-based treatment of chronic pain. The patient focuses their attention on uncomfortable physical sensations with no attempt to alter them, instead developing compassion toward both positive and aversive bodily experiences [114, 115]. Neuroimaging studies support the notion that MBSR strategies have allowed patients to adopt a new perception of their chronic pain. The chronic pain experience involves the interplay of nociceptive cues, cognitive distortions, and negative emotional appraisal. Compared to controls, subjects receiving mindfulness instruction showed reduced activity in the right amygdala, parahippocampus, and insula, and increased activation in the dorsomedial and other PFC subregions during the presentation of unpleasant visual stimuli, consistent with attenuated emotional activation [116]. Mindfulness training has also been shown to reduce pain severity and uncouple pain from opioid use by helping the patient attenuate negative appraisals, reduce fixation and hypervigilance from chronic pain, and reduce pain catastrophizing [86, 107, 117–120]. As in SUD, MBSR interventions help to disengage the cycle of maladaptive pain coping strategies and prevent related behaviors, such as opiate stockpiling and other habits [107]. Together, these lines of evidence suggest that mindfulness-based therapeutic interventions hold great promise for treating and preventing OUDs, chronic pain, and co-expression of both, and the authors hypothesize that the biopsychosocial nature of the approach is key to its effectiveness.

5.3 Solution-focused brief psychotherapy (SFBP)

Solution-focused brief psychotherapy (SFBP) applies a postmodern constructivist approach to counseling, meaning that an individual's experience of their substance use acts as the "objective truth" [121]. In this way, the therapist will collaborate with the client in order to develop a working, clinical understanding of the client's problem situation in terms of experience, perception, and meaning related to ambiguous stimuli and events [122]. Like CBT and MBSR, SFBP hinges on the development of a personalized construction of the problem behaviors or experiences and reframing of meaning that perpetuates maladaptive cycles of thought and behavior. Some researchers believe that it is not the specific interventions, but the demeanor and actions of the therapist that promote the therapeutic effects of solution-focused therapy. The collaborative relationship extended by the therapist, use of core facilitative conditions of the counseling process, mindfulness of the stages of change, and a focus on solutions instead of problems provides moderate empirical backing [123–125]. SFBP practitioners believe that therapy relies on the therapist's ability to engage the client in examining their negative *status quo* and that they become aware of exceptions to problem situations so as to direct insight toward future change [126]. SFBP allows the client to determine their own goals related to recovery, which includes harm-reduction strategies, and does not rely upon all-or-nothing measures such as complete abstinence from drugs.

Many reports support the notion that solution-focused brief psychotherapy (SFBP) has worked well for individuals with SUD, and more modern group-based SFBP approaches have continued to be successful [121, 122, 127]. Although research has stagnated somewhat, SFBP group therapy appears to be effective for treating SUD, sometimes outperforming traditional programs [127]. This success may lie in allowing patients to choose their own goal structures and giving them more responsibility, which generally increases the likelihood of a positive therapeutic alliance between clinician and patient and typically yields better treatment outcomes [127]. Because depression and anxiety, like chronic pain, are highly comorbid with SUD, clinicians have had more success in targeting these disorders in order to address the other habitual drug-seeking behaviors [122, 127] and solution-focused techniques have been found to outperform traditional therapies in this regard [127]. Specifically, interpersonal functioning, symptom severity, and social roles pre- and post- treatment, have shown improvements in those receiving solution-focused interventions [127–129]. Meta-analyses have also shown that 23% of systematic reviews have reported positive trends in depression-related outcomes [130, 131]. Applying a solution-focused mindset to other psychotherapies, including CBT and MBSR, has also led to positive outcomes in the treatment of SUD and depression [127, 132]. Another advantage of SFBP is its cost effectiveness, due to its brief duration yet surprisingly long-term positive outcomes for many. Although no studies to date have examined the efficacy of SFBP specifically for the treatment of OUD, application of this approach to OUD seems promising.

In the context of chronic pain, the emphasis of solution-searching in SFBP may be advantageous, as individuals living with chronic pain typically react passively to their pain sensations, or develop coping strategies that can be misguided or unhelpful [133]. The idea of a "preferred future," a concept at the core of SFBP wherein the therapist assists the patient in identifying exceptions to their painful *status quo*, has elicited unique responses from patients often lacking in hope [126, 133]. Research on the therapeutic effects of SFBP for chronic pain is quite limited. However, SFBP has been helpful when coupled with physical rehabilitative practices. Two studies have shown improvement of individuals undergoing orthopedic rehabilitation while on sick leave, with over 60% of participants returning to homeostatic daily functioning levels as a result of solution-focused practices, as opposed to a 13% return rate from the waitlisted control groups [134, 135]. A case study also supports the efficacy of combined biofeedback (galvanic skin response) and SFBP in order to manage chronic pain associated with gastro-esophageal reflux disease, with the patient showing a significant decrease in chest pain and increase in personal life satisfaction lasting two months post-treatment [136]. Further research on biopsychological interventions such as combining biofeedback with SFBP for chronic pain could be illuminating.

5.4 Motivational interviewing (MI)

Originally developed by Dr. William Miller for alcohol use disorders in 1983, motivational interviewing (MI) can be described as a therapeutic conversation, held by the therapist and client, about aspects of change [137]. Therapists use specific communication strategies that allow the client to explore their arguments for why change is not possible, seeking to elicit "change talk" from the client by developing discrepancies in the way the client thinks and speaks about their issues. These discrepancies arise from a collaborative exploration of the client's story pertaining to how substance use, for example, has impacted their lives. The therapist's role is to highlight ambivalence that has arisen from the storytelling and provide space for the client to think about what changes they are capable of making [138]. Eventually,

by weighing personalized positive and negative aspects related to change outcomes, the client breaks down the lines of logic sustaining pathological behaviors [139, 140]. MI addresses four processes: engaging, focusing, evoking, and planning [141]. Engaging the client in a person-centered style develops the therapeutic bond that will facilitate change [141]. Focus revolves around the change target of the client, which is developed collaboratively to avoid negative power dynamics, polarization, or fractures to the therapeutic relationship [142]. Evocation involves intentional change talk wherein the client must identify their own personal reasons for change and therapist feedback aims to prevent potential losses in motivation related to these reasons. Planning involves collaboration and commitment as the primary method for enforcing the desired change. The ability for the client to elicit their own motivations for change rather than the therapist imposing their own advice is the driving force of this therapy.

MI has become one of the leading theoretical interventions for treating individuals with SUD. Some early explanations of its popularity are its cost effectiveness, theoretical fluidity, usefulness for non-treatment-seeking populations, and motivational enhancement of the client, which is highly important in addiction treatment [143, 144]. Although there have only been a handful of studies, MI has shown clinical efficacy in the treatment of a variety of SUD [143, 145]. For example, the ability to resolve ambivalence related to drug use and to reframe one's perspective of change ultimately reduced active drug use to a larger extent in an MI group compared to a more confrontational counseling style focused on the consequences of risky drug use [138, 139, 146]. Change talk has been shown to play a vital role in treatment outcomes and researchers have hypothesized that it promotes a neurocognitive shift negatively correlated with substance use [147, 148]. For example, an fMRI study showed that positive change talk inhibited activation of reward circuitry by alcohol-associated cues, suggesting that change talk can nullify reward activation under high-risk circumstances and thereby prevent cue-induced relapse [147, 149]. A single-blinded, randomly controlled trial found that bimonthly MI treatment significantly reduced the number of opioid overdose events and promoted a lower attrition rate amongst participants [150] compared to psychoeducation and tertiary prevention strategies [150, 151]. Educational programs did reduce other risk factors, such as viral infections as a result of needle misuse and enhanced protective factors including how to detect overdose, promotion of needle exchanges, and safe injection habits [151]. Future studies examining potential benefits of combined pharmacological and MI methods on treatment outcomes for patients with OUD will be important.

Although controlled studies have been limited by the fluidity of motivational strategies and their implementation, researchers have found that MI can augment treatment of chronic pain, and is moderately effective for lower-back pain, asthma, hypertension, cardiac and respiratory issues, and fibromyalgia [152]. In this context, the focus of MI is on resolving ambivalence through change talk and enhancing the ability to cope with chronic pain by incorporating mindfulness and cognitive restructuring techniques [153–155]. In addition, MI interventions used in conjunction with physiotherapy enhance the therapeutic relationship between the physician and patient, which correlates to more positive outcome expectancies of the patient that ultimately decrease subjective pain intensity and increase range in physical functioning [156]. Another study found that infusing a biopsychosocial assessment of chronic pain with MI also had more favorable outcomes, including marital satisfaction, reductions in pain intensity, stability in positive mood, lower ratings of personal distress, and higher ratings of empathy [155]. Future studies examining the efficacy of MI in treating comorbid SUD and chronic pain would be informative.

6. Conclusions

Chronic pain and addiction are widespread, pervasive, and significant public health burdens that demonstrate a need for more effective management strategies. The known effectiveness of opioids for managing acute pain combined with the limited therapeutic alternatives for chronic pain, have led to an overreliance on opioids for long-term pain management and the current opioid crisis in the United States [2]. In this chapter, the authors have discussed conceptualizing chronic pain and SUD using a similar biopsychosocial framework and suggest that both can be more effectively managed by including clinical mental health therapeutic techniques as opposed to a purely biomedical approach. While psychotherapy has long been used in treating SUD, applying these techniques to chronic pain is fairly novel. Evidence of the effectiveness of these nonpharmacological treatments for chronic pain, particularly for long-term management, is still sparse [157]. However, the techniques highlighted in this review, CBT, MBSR, SFBP, and MI are promising in managing mental illnesses that are frequently comorbid with chronic pain, suggesting further research into their efficacy for chronic pain is warranted. Moreover, the biopsychosocial parallels between chronic pain and SUD represent potential areas of translational research to further improve these nonpharmacological pain management practices and foment social change. By addressing these areas of biopsychosocial overlap, nonpharmacological approaches may hold great promise in reducing the negative impacts of chronic pain and the opioid epidemic simultaneously.

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