Prevalence, Causes, and Treatment of Substance Use Disorders: A Primer

Spencer Bujarski Ph.D.¹, Aaron C. Lim M.A.¹, & Lara A. Ray Ph.D.¹,²

1. University of California Los Angeles, Department of Psychology
2. University of California, Los Angeles, Department of Psychiatry and Biobehavioral Sciences

Corresponding Author: Spencer Bujarski, Ph.D., University of California, Los Angeles, Psychology Department, 502 Portola Plaza #1285 Franz Hall Los Angeles, CA 90095 United States; Email: SBujarski@psych.ucla.edu

Citation:
Abstract
Drug and alcohol addiction are among the most prevalent and costly psychiatric disorders, particularly in the context of the criminal justice system. In this article we provide an overview of the science of addiction focusing on the diagnosis of substance use disorder, the brain processes that lead to addiction, the risk factors that increase risk for addiction, and concluded with a review of the available behavioral and medical treatments.
Introduction

Substance use disorders are common and costly psychiatric disorders. According to the 2016 National Survey on Drug Use and Health (NSDUH), an estimated 51.3 million Americans aged 12 or older were current cigarette smokers, 136.7 million people were current alcohol drinkers, and 28.6 million people reported using an illicit drug in the past 30 days. Among illicit drugs, marijuana use was most common (24 million), followed by prescription pain relievers (3.3 million). While cigarette smoking has become less prevalent in recent years, illicit drug and alcohol use has increased.

Drug and alcohol abuse also carries large societal costs. Alcohol use alone is estimated to cost more than $200 billion in the United States with binge drinking accounting for 70% of that cost (typically defined as 5+ drinks for men and 4+ for women). Opioid abuse has recently gained national attention as a public health crisis with dramatic increases in the number of opioid overdose deaths over the past two decades. In 2016 alone, an estimated total of 64,000 people died from a drug overdose in the US and opioids such as Fentanyl, Heroin, and other prescription opioids accounting for approximately three quarters of those deaths. In the context of the criminal justice system, drug use and addiction are major factors. According to a 2012 report from the Bureau of Justice Statistics, drug law violations were the most common criminal offense among correctional populations and parolees. Furthermore, approximately half of state and federal prisoners meet diagnostic criteria for a substance use disorder, yet only 20% of those who need treatment receive it. The need for more effective recognition and management of drug use and addiction within the criminal justice system is essential. In this article, we provide an introduction to the diagnosis, causes, and effective treatments for addictive disorders.

Diagnosis

Among the millions of Americans who use drugs and alcohol, a subset meets diagnostic criteria for addiction, otherwise known as a substance use disorder (SUD). Though there are several classification systems for diagnosing an SUD, within the US the most commonly used system for all psychiatric diagnoses is the Diagnostic and Statistical Manual for Mental Disorders (DSM), published by the
American Psychiatric Association (APA). The fifth and most recent edition of the DSM was themes: 1) loss of control over substance use, such as using the substance for excessive amounts of time or using much more than intended; 2) social harms, including neglecting major responsibilities at work or at home, and having persistent arguments with others about substance use; 3) risky use that may result in physical harm, such as recurrent use of a substance while operating a motor vehicle or continued use despite knowledge that it exacerbates an identified physical condition; and 4) physiological dependence, where the individual requires increasing amounts of the substance to achieve the same effect (tolerance) and experiences substance-specific withdrawal symptoms when not using.

A diagnostic SUD assessment typically involves a clinical interview wherein a trained clinician will assess each of the 11 symptoms and patients must meet criteria for two or more symptoms to be diagnosed with an SUD. Additionally, in DSM-5 an SUD diagnosis is accompanied by a severity specification ranging from mild (2-3 symptoms), moderate (4-5 symptoms) and severe (6+ symptoms). According to the 2016 NSDUH survey approximately 20.1 million people met criteria for a SUD in the past year including 15.1 million who had an alcohol use disorder and 7.4 million who had an illicit SUD.

Diagnostic clinical interviews are frequently supplemented by a toxicology screening to verify patients’ substance use using biological verification. For alcohol use, a breath alcohol concentration (BrAC) test is often performed along with more novel tests of alcohol metabolites in blood and urine samples, which in turn allow for the assessment of longer time periods of alcohol use.

A Pathology of Choice and Control

Drugs of abuse are powerful psychoactive agents that are capable of producing dramatic short-term changes in brain function (e.g. the short-term euphoric effects of a drug). More importantly to the development of chronic SUD however, is the fact that drugs are able to produce substantial and long-lasting changes in brain structure, organization and function, a process called neuroadaptation. A central focus of neuroscientific research on addiction is understanding the neuroadaptive changes caused by various drugs of abuse. While there exists drug specific neuroadaptive responses, there are also several
key neuroadaptations that are shared across drug classes and are hypothesized to produce the clinical symptoms of SUD.

One prominent and well-supported neuroscientific theory of addiction highlights two interrelated neuroadaptations. First, neuroadaptation in the mesocorticolimbic dopamine reward circuitry produce a state whereby drugs and the stimuli associated with drugs such as liquor stores, advertisements, and drug using peers acquire pathologically high reinforcing value. This means that, in the addicted state, the individual experiences intense desire to obtain and consume the individual’s drug of choice, or cravings. Simultaneously, neuroadaptation in the prefrontal cortex leads to impairment in brain regions responsible for controlling impulsive behavior. Put together, drugs of abuse are able to produce changes in brain function that leads to impairment in both the brains “go” system (intense drug cravings), and in the brains “stop” system (deficient impulse control). In this way SUD can be conceptualized as a brain-based pathology affecting both the individual's drive to consume drugs as well as their capacity to successfully execute volitional control over that drive. Of note, these neuroadaptive changes are largely not permanent, though they can take a long time to reverse and can quickly re-emerge in the context of a relapse. Thus, the current understanding of addiction science suggests that decision-making processes are impaired by chronic substance use. However, these changes are not necessarily sufficient to absolve the user of responsibility for their actions as evidenced by the fact that chronic drug users can, and do, make changes to their behavior, particularly with proper intervention.

Risk Factors for Addiction

Family History

It has long been recognized that addiction tends to run in families. Having a parent, sibling, or grandparent with an SUD is one of the most predictive risk factors for addiction. Family history is also one of the easiest risk factors to assess in clinical and legal settings. Historically, the familial transmission of addiction has been particularly true among men, however some recent evidence has suggested that the familial transmission of addiction with women has been increasing in recent decades. Genetics certainly
represents one major factor explaining the familial risk, however other psychological factors such as poverty, stress, and exposure to trauma also represent risk factors that tend to be passed down through generations.

*Genetics*

Genetics appears to play a large role in determining who is likely to develop an SUD. Through studying identical versus fraternal twins and biological versus adopted siblings, researchers have estimated that over half of the liability for SUD is attributable to genetics. These studies have also demonstrated that the genetic risk factors for SUD are generally shared across different drug classes, with a small subset of genetic risk factors being unique to individual substances (e.g. through affecting metabolism of a particular drug). Furthermore, the genetic factors conferring risk for SUD also appear to confer risk for other externalizing disorders such as conduct disorder in children and antisocial personality disorder in adults, both of which are major risk factors for criminality.

While there is considerable and convincing evidence supporting the importance of inheritance writ large, less is known about which specific genetic variants confer risk for a given individual. Spurred by the rapid technological advances in genetic testing and DNA sequencing over the past two decades, geneticists have utilized a number of methods to explore which genes are related to SUD. Considerable research has explored mutations in genes associated with neurobiological systems thought to play a central role in addiction (e.g. GABA, glutamate, dopamine, acetylcholine, and opioids), however findings have been relatively inconsistent. What has become clear is that the genetics of SUD, and indeed the vast majority of psychiatric illnesses, are complex insofar as they are related to many different gene variants, each of which might only have a small effect, but when present in combination produce the large heritability observed in population statistics. Further adding to this complexity, some studies have shown that genetic variants may relate to addiction risk only in the presence of environmental factors such as traumatic experiences.
Trauma

Exposure to traumatic events including sexual abuse, physical abuse and the emergence of posttraumatic stress disorder (PTSD) dramatically increase the risk for SUD. Among adolescents, some evidence suggests that the effect of trauma with respect to SUD may be greater among young women than young men, though evidence for this sex difference is mixed. In general men are significantly more likely to have an SUD regardless of traumatic history, accounting for 60-70% of those with a substance use disorder. Thus, this elevated prevalence overall may obscure some of the risk associated with traumatic exposure. Furthermore, there may be differences in the willingness of young men and women to report traumatic experiences. When studies use multiple approaches to assess for trauma that reduce the likelihood of reporting bias, traumatic exposure, particularly in childhood, predicts more drug use, and more SUD among both men and women.

PTSD is one of the most common co-occurring psychiatric disorder for patients with SUD. In fact, among the subset of patients who seek addiction treatment, 12-34% present with comorbid PTSD. This rate is even higher for women where approximately half of women seeking SUD treatment meet criteria for PTSD. PTSD represents the extreme in terms of the psychological effects of trauma and is characterized by a cluster of symptoms including intrusive and unwanted re-experiencing of the traumatic incident(s), avoidance of trauma cues, negative alterations in mood and thought patterns, and hyperarousal. When PTSD occurs prior to the SUD, patients typically report using substances to “numb” the highly aversive symptoms of PTSD. However, in some cases, substance abuse precedes PTSD, and in fact chronic drug abuse can increase the chances for traumatic incidents through increasingly risky behavior.

Psychiatric Comorbidity

The co-occurrence of SUD with another psychiatric disorder is very common at approximately 50%. Among those seeking treatment, the rates and severity of these comorbidities are often higher. Furthermore, the presence of SUD and a comorbid psychiatric disorder is associated with poorer
prognosis and treatment outcomes for both conditions. Often comorbid conditions are undertreated in the context of a SUD, owing in part to the perception that addicted patients are unreliable, unmotivated, or otherwise irresponsible. Conversely, those patients receiving specialty addiction treatment are frequently not adequately evaluated and treated for co-occurring conditions.

Some evidence exists to support the hypothesis that comorbidity is a result of attempts to “self-medicate.” For example, high rates of nicotine abuse among patients with schizophrenia may be a consequence of nicotine’s effects on dopamine which has been shown to be deficient in schizophrenia. Furthermore, high rates of alcohol abuse among patients presenting with anxiety disorders or PTSD may be due to acute anxiolytic effects of alcohol. In fact, alcohol affects GABA receptors in a similar fashion to benzodiazepines, a widely prescribed class of anti-anxiety medications that includes Xanax and Valium. The self-medication hypothesis however does not fully explain the extent of psychiatric comorbidity. For some patients, their drug use actually increases the severity of their other psychopathology. It is also common for substance abuse to precede the onset of comorbid psychopathology, flipping the “self-medication” hypothesis upside down. One particularly salient example is that, among those with a family history of schizophrenia, marijuana use may increase the risk of psychotic symptoms. Other hypotheses exist to explain the high rates of comorbidity, including that both disorders are a consequence of a shared risk factors, however more research is needed to disentangle which hypotheses apply to which individuals.

Treatment

Among the 19.9 million adults in the US who met criteria for SUD and/or needed substance use treatment in 2016, only 2.1 million (or 11%) actually received specialty treatment for addiction. These disheartening statistics highlight both the need to develop effective addiction treatments and the need for broad outreach.

Behavioral Treatments
There are multiple behavioral/psychotherapy treatments for SUD. Twelve-step programs, such as Alcoholics Anonymous (AA), are implemented internationally to treat various SUDs. They offer recovering individuals social and emotional support utilizing the 12-step framework. Broadly, the steps emphasize values of humility, accountability, recognition of a higher power, and achieving abstinence through conscious reflection on their substance use. Of note however, there exists wide variability between individual 12-step groups, including on issues such as member expectations, social structure, and therapeutic emphasis. In general, the scientific community now accepts mutual health groups, such as AA, as having empirical support. In other words, it has been demonstrated scientifically that AA is superior to no treatment, and comparable to Cognitive Behavioral Therapy (CBT).

In CBT, individuals collaborate with a therapist to replace substance use with less maladaptive and more goal-oriented behaviors. CBT can be administered in group or individual format. CBT programs include education about substance use and addiction, scheduled changes in activities that serve individualized life goals instead of substance use (e.g. monitoring and maintaining a natural sleep routine rather than utilizing drugs to fall asleep or wake up), and preparation for withstanding cravings by developing alternative reactions (e.g. focusing on the negative aspects of withdrawal to buffer against cravings to use). Across many studies CBT has been shown to be an effective SUD treatment.

Motivational Interviewing/Enhancement (MI, or MET) primarily addresses motivational barriers in pursuing treatment among individuals with SUD. Specifically, MI targets ambivalence about large behavior changes by probing and challenging individuals’ beliefs about SUD consequences and their ability to successfully make large lifestyle changes. MI can be used either as a standalone or adjunct treatment. It is most effective for individuals at lower levels of SUD severity. Individuals with more severe SUD typically require more intensive treatment such as 12-step, or CBT.

Another treatment for SUD is contingency management, which is grounded in rewarding biologically-verified abstinence from substances with vouchers or compensation. This process reinforces individuals to engage in non-substance related behaviors while simultaneously reducing the relative reinforcing value of substances. Contingency management has been found in a meta-analysis to be
moderately effective in treating various SUDs. A limitation of this treatment, however, is the financial and structural resources required to continuously reward individuals; some studies have found that using a lottery system (e.g. having a chance to earn a reward rather than direct payment) is one way to address this limitation.

Lastly, therapies based on meditative and mindfulness practices have recently been developed as treatment options for SUD. Such therapies are designed to increase and promote awareness of the “here and now” to cope with distressful experiences of substance cessation. For example, Mindfulness-Based Relapse Prevention helps individuals cope with craving by increasing awareness of their initial response to craving in a non-judgmental manner. Individuals can subsequently learn to focus on the transient nature of cravings and develop alternative responses to craving. Preliminary work suggests that mindfulness techniques are promising, but further research is required to establish their efficacy in treating SUD.

In summary, behavioral treatments for alcohol and drug addiction have strong scientific support when compared to no treatment and increasing access to behavioral interventions is expected to markedly increase chances for recovery and reduce the negative consequences of addiction.

Medical Treatment for Alcohol Use Disorder

Several medications are regularly used for the management of short-term withdrawal from drugs of abuse, with the aim of stabilizing patients in an abstinent state, termed detoxification. However, given the chronic and relapsing nature of addiction which persist far beyond the management of acute withdrawal, here we will focus on the long-term medical treatment approaches for patients with an SUD.

Currently only three medications are FDA approved for the treatment of alcohol use disorder. The first, disulfiram (trade name Antabuse) acts through blocking the normal metabolism of alcohol. Specifically, disulfiram blocks an enzyme in the liver that breaks down alcohol’s primary metabolite, acetaldehyde. Acetaldehyde, particularly at high levels can be toxic and produces dramatic aversive reactions in the body including flushing, nausea, vomiting, and throbbing headaches, among other symptoms. Therefore, consumption of even small amounts of alcohol while on disulfiram produces these
highly aversive symptoms. In this way, disulfiram leads to a strong motivation for patients not to drink. In highly structured and supervised settings, disulfiram can be effective in managing alcohol use disorder, however in outpatient settings adherence to proper disulfiram dosing is often extremely low and thus disulfiram has not been shown to be an effective long-term outpatient treatment.

Naltrexone (trade name ReVia [oral dosing] and Vivitrol [injectable]) is an opioid antagonist, meaning that it blocks the function of opioid receptors in the brain. Neuroscience research has shown that alcohol produces much of its euphoric effects through indirectly stimulating the release of opioid neurotransmitters. Thus, by blocking opioid receptors, naltrexone reduces the pleasurable effects of alcohol (without producing the strong aversive reaction of disulfiram) and reduces alcohol cravings. In clinical trials, naltrexone, both oral and injectable, significantly reduces the risk of relapse and in particular reduces the intensity of drinking to safer limits that do not carry the same health and social risks of very heavy drinking. Not all patients see clinical benefit from naltrexone however, and some in the field have suggested that naltrexone may be more effective for a subset of patients based on characteristics such as the subtype of alcoholism and genetic factors. Though the clinical effects for naltrexone are moderate on average, naltrexone is still considered the first line medical treatment for patients with alcohol use disorder.

Lastly, acamprosate (trade name Campral) acts on multiple neurotransmitter systems including glutamate and GABA, the brain's primary excitatory and inhibitory neurotransmitter systems. Chronic alcoholism is thought to produce neuroadaptations in these systems that result in a chronic imbalance between excitation and inhibition. By affecting glutamate and GABA receptors, acamprosate is thought to reduce withdrawal symptoms, such as sleep difficulty, agitation, and anxiety which can persist for much longer than the short-term symptoms managed in detoxification. Of note however, clinical efficacy for acamprosate appears to be greater in studies conducted in Europe versus the US.

*Medical Treatments for Opioid Use Disorder*
FDA-approved medical treatments for opioid use disorder include methadone, buprenorphine, and extended-release naltrexone. These medications have been shown to reduce the risk of relapse to opioid abuse, and are helpful in managing cravings. Methadone is a synthetic opioid agonist, meaning that it stimulates opioid receptors and thus alters the brain’s responses to pain and blocks the “high” effect of abused illicit and prescription opioids. Methadone has been studied and utilized as a treatment for decades and demonstrates positive long-term opioid use outcomes (i.e. over 6 months post-treatment completion), even when it is provided without adjunct behavioral counseling. Of note however, methadone treatment requires highly structured specialty clinics with specific clinical training and infrastructure.

Buprenorphine works as a partial agonist for mu-opioid receptors and antagonist kappa opioid receptors, and produces sensations of euphoria and/or respiratory depression that are similar to abused opioids. Unlike abused opioids, however, buprenorphine’s effects are relatively weak and level off quickly thus reducing the risk of abuse. Buprenorphine is available in two primary forms; it can be taken alone (trade name Subutex®) or in combination with naloxone (trade name Suboxone®), an opioid receptor antagonist chemically similar to naltrexone and used extensively to prevent opioid overdoses. This latter formulation was designed to prevent individuals from misusing the medication; if individuals attempt to inject suboxone intravenously, or otherwise alter the medication, the naloxone blocks the effect of the buprenorphine. In this way, individuals who take Suboxone are less likely to “divert”, or misuse the treatment to further their addiction. Recent reviews of suboxone have overwhelmingly demonstrated the clinical benefit of buprenorphine for the treatment of opioid use disorder.

Extended-release naltrexone is an injectable treatment for opioid use disorder that can be administered on a monthly basis. Like its effects with alcohol, naltrexone blocks the euphoric effects of opioids and has been shown to be effective in preventing relapse among criminal justice defenders. A recent multi-site clinical trial found that individuals who received extended-release naltrexone were almost half as likely to return to regular opioid use as those not on Vivitrol. Other important outcomes such as use of other substances, unsafe sexual behavior, and reincarceration rates, did not differ between those who did and did not use extended-release naltrexone however. These results underscore the
challenge of providing effective substance use treatment for populations with multiple risk behaviors, as well as the importance of providing such treatment within broader rehabilitation efforts.

Opiate use disorder continues to be a growing trend and national health concern driving increased attention and efforts for opioid abuse treatment development. In fact, identifying novel medical treatment options for opiate use disorder is one of the three top priorities of the U.S. Department of Health and Human Services. With these efforts, regular adherence to FDA-approved medications coupled with behavioral counseling provides the highest chance of recovery for individuals with opiate use disorder.

*Medical Treatments for Other Illicit Drugs*

While a great number of individuals struggle with the misuse of other illicit drugs such as marijuana, methamphetamine, and cocaine, there are no FDA-approved medications for non-alcohol or -opioid addiction. Identifying effective treatments for these other SUDs represents an important focus for addiction researchers internationally.

*Off-Label Treatments*

Partly due to scarcity of FDA approved medications for SUD indications, many physicians treat patients using off-label prescriptions. Most commonly, off-label prescriptions are those that are written for currently available medications, but prescribed for an indication that has not been approved by the FDA. For example, an antidepressant may be prescribed for a substance abusing patient who struggles with depressed mood that is often observed in severe and chronic addiction. Other times, providers may write prescriptions for medications which are currently being investigated as possible treatments for an SUD (e.g. topiramate, baclofen, varenicline, and gabapentin) based on the early evidence that these medications may be effective SUD medications. Ongoing studies are testing a host of novel compounds for addiction aiming to provide patients with effective and ultimately personalized treatment options. Off-label prescription practices are often bolstered by the individual providers’ clinical impression on the effectiveness of a medication for those patients in their care. While there are clear benefits to providers
treating SUD patients based on their best clinical judgement, there is also risk to the widespread prescribing of medications that have not proved clinical benefit to the high standards set by the FDA and other regulating bodies. While some of these medications may ultimately demonstrate reliable clinical benefit in randomized clinical trials, many will be shown to produce outcomes no better than a placebo while carrying significant risk for side-effects.

Conclusion

In the US and worldwide alcohol and drug addiction are common, costly, and impactful. Particularly in the context of the judicial system, the addiction is often central to many cases. Historically, addiction has been viewed as a moral failing or personal weakness which has significantly impacted how addiction is treated in legal contexts, often leading to overly punitive sentences. In this article we have reviewed the science of addiction focusing on the diagnosis of substance use disorder, the brain processes that lead to addiction and concluded with a review of the available treatments for drug and alcohol addiction. While there is certainly more research to be done to fully understand the causes of addiction and develop effective and targeted treatments, two areas of consensus are worth noting: First, addiction is generally accepted in the field as a brain-based disease that is influenced by factors such as their genetics and traumatic history. Second, empirically supported behavioral and medical treatments exist, and when individuals engage with these treatments, they are effective in helping patients curb their drug and alcohol abuse. A common understanding of addiction treatment is that treatment does not need to be voluntary in order to be effective. To that end, mandated treatments may provide individuals with opportunities to address their substance use regardless of whether the individual voluntarily engages in treatment. As scientists involved in developing novel treatment strategies, it is imperative that more members of society affected by addiction continue to have the opportunity to benefit from these treatments and mandated interventions are an important way in which individuals become more aware of their substance use problems and engage with treatment.
Citations


T.H. Moore et al., Cannabis use and risk of psychotic or affective mental health outcomes: a systematic review, 370 The Lancet 319–328 (2007).


National Survey on Drug Use and Health (U.S.) and the United States: Key substance use and mental health indicators in the United States: Results from the 2016 National Survey on Drug Use and Health (SMA 17-5044) (2017).