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The Cognitive Neuroscience and Pharmacotherapy Associated With Drug Dependence

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ABSTRACT

Drug dependence is a serious health hazard and social issue today. It has now become more widely recognized clinical disorder and the severity of the problem been fully realized. Various factors are responsible for this. These include low income, little education. Social pressure is a common causing factor in adolescents. Dependence over a time can also cause tolerance. Options for treatment and being analyzed and treatment is being promoted to overcome this disease that is becoming a common occurrence today. Dependence has caused multiple deaths in The United States averaging to 17,000 deaths a year due to overdose. This review examines the neurological effect that drug dependence causes. It discusses how chronic, use of opioids induces adaptive changes that— the "drug-dependent" state. These abnormalities in are complex and long-lasting. Various treatments that have come into practice today to relieve patients from this addiction. Pharmacological therapy with methadone, modafinil, topiramate, or other medications directly offsets or reverse the changes in the brain associated with addiction. Along with pharmacotherapies, therapies like ‘peer support groups’ are also being encouraged.

INTRODUCTION

[1]Drug dependence is defined as a drug-induced state in which, upon cessation of the drug, physical and/or psychological withdrawal symptoms occur. Drug dependence is not a unique phenomenon to opioids, as psychostimulants and other drugs of abuse can elicit an abstinence syndrome. Like opioids, psychostimulant abstinence precipitates dysphoria, emotional withdrawal, and hypo-dopaminergic tone, but opioids may trigger different vulnerabilities for addiction and relapse.

[2]There is evidence across a range of other substances—including marijuana, cocaine, other psychostimulants, and inhalants—that the risk of developing dependence or abuse is greater for individuals who initiate use of these substances in adolescence or early adolescence than for those who initiate use during adulthood. Initiating substance use during childhood or adolescence is linked to substantial long-term health risks. Early (aged 12 to 14) to late (aged 15 to 17) adolescence is generally regarded as a critical risk period for the initiation of alcohol use, with multiple studies showing associations between age at first alcohol use and the occurrence of alcohol abuse or dependence. For example, 2012 National Survey on Drug Use and Health data indicate that among those adults who first tried marijuana at the age of 14 or younger, 13.2 percent were classified with illicit drug dependence or abuse; this percentage was 6 times higher than that for adults who first used marijuana at the age of 18 or older.In fact, among adolescents, the transition from initiation to regular use of alcohol, marijuana, and other drugs often occurs within 3 years. Examining patterns in the age of drug or alcohol initiation among persons in treatment for substance abuse may increase understanding of the characteristics of those who initiate substance use during their childhood or adolescence and highlight potential ways to optimize prevention and treatment efforts.

The Treatment Episode Data Set (TEDS) is a national data system of annual admissions to substance abuse treatment facilities. It has data on the age of initiation for up to three substances of abuse per admission.

[3]Many common factors also link pregnant women most at risk for drug abuse. These include low income, little education, absence of insurance or dependence on Medicaid, single status, and residence within the inner city. Because of confounding factors, and the presence of comorbidities such as malnutrition and sexually transmitted diseases, it is difficult to assess the ill effects suffered by the fetus and neonate.

[4]An opioid epidemic has emerged over the past decade in the United States causing overdose deaths fast approaching numbers dying from car accidents, with about 17,000 annual deaths from opioid therapeutics and 8200 deaths from heroin overdose in 2014. Sales of prescription medications have skyrocketed, with an increase in retail sales of 1293% for methadone, 866% for oxycodone, and 525% for fentanyl from 1997–2007. Similarly, the increase in therapeutic opioid use in the United States in milligrams per person increased 402% from 1997 to 2007. Although reformulation of oxycodone to an abuse-deterrent form has helped curb the oxycodone epidemic, the migration to other opioids following drug dependence remains problematic, especially the migration to heroin. The statistics are disturbing, and in 2011, the White House released an action plan entitled "Epidemic: Responding to America's Prescription Drug Abuse Crisis". Although opioid therapeutic prescriptions for pain are largely blamed for creating the epidemic, other factors undoubtedly contribute to the problem, including the low price of heroin and environmental stressors leading to anxiety and depressive states. The conundrum of effective treatment of pain while minimizing opioid prescription abuse is a major political challenge that remains unresolved.

[5]Cannabis is globally the most commonly used psychoactive substance under international control. In 2013, an estimated 181.8 million people aged 15-64 years used cannabis for nonmedical purposes globally. There is an increasing demand of treatment of cannabis use disorders and associated health conditions and there has been increased attention to the public health aspects of cannabis use and related disorders in international drug policy dialogues. This publication builds on contributions from a broad range of experts and researchers from different parts of the world. It aims to present the current knowledge on the impact of nonmedical cannabis use on health.

[6]Brain abnormalities resulting from chronic use of heroin, oxycodone, and other morphine-derived drugs are underlying causes of opioid dependence (the need to keep taking drugs to avoid a withdrawal syndrome) and addiction (intense drug craving and compulsive use). The abnormalities that produce dependence, well understood by science, appear to resolve after detoxification, within days or weeks after opioid use stops. The abnormalities that produce addiction, however, are more wide-ranging, complex, and long-lasting. They may involve an interaction of environmental effects—for example, stress, the social context of initial opiate use, and psychological conditioning—and a genetic predisposition in the form of brain pathways that were abnormal even before the first dose of opioid was taken. Such

abnormalities can produce craving that leads to relapse months or years after the individual is no longer opioid dependent.

[7]Based on extensive investigations of rodent and primate models, the mesoaccumbens dopamine pathway, extending from the ventral tegmentum of the midbrain (VT) to the nucleus accumbens, appears to be the critical shared substrate of the reinforcing effects of cocaine (Louilot et al., 1989; Williams, 1989; Apicella et al., 1991; Schultz et al., 1992) and other addictive drugs (reviewed in Koob, 1996). Using non-drug stimuli, the nucleus accumbens has also been shown to play a critical role in learning associated with reinforcement (Mirenowicz and Schultz, 1996). Reinforcement in animals depends on the increase in synaptic dopamine levels in the mesoaccumbens circuit produced by cocaine-like drugs via blockade of the dopamine reuptake transporter (DAT) (DeWit and Wise, 1977; Ritz et al., 1987). In both animals and humans, the acutely reinforcing effects of psychostimulant drugs can produce a pattern of repeated self-administration. Human users may initially self-administer cocaine to gain pleasure, to conform to peer behavior, or to relieve stress and other dysphoric feelings. An accelerated pattern of drug use in vulnerable individuals may produce increasing levels of dependence and, eventually, addiction (Hyman, 1996).

Neurobiology of the brain and causes of dependence

[8]While the mesoaccumbens dopamine pathway has been most closely implicated in the acutely rewarding actions of cocaine, other circuits have also been implicated in reward processes, including the basal forebrain, which receives major afferents from the nucleus accumbens and itself receives dopaminergic input (Heimer et al., 1997). Brain stimulation reward (BSR) experiments have directly implicated the basal forebrain in reinforcement (Rompre and Shizgal, 1986; Shizgal et al., 1989; Arvanitogiannis et al, 1996). The nucleus accumbens is also strongly linked to the amygdala (Ito et al., 1974; Yim and Mogenson, 1982; Russchen et al., 1985; Amaral, et al., 1992), a linkage thought to be important for the formation of stimulus-reward associations (Jones and Mishkin, 1972; Spiegler and Mishkin, 1981; Gaffan and Harrison, 1987; Gaffan et al., 1988). Recently, PET scanning has demonstrated amygdala activation during cocaine craving in abstinent cocaine-abusing subjects relative to normal controls (Childress et al., 1996, Soc. Neurosci., abstract; Grant et al., 1996; Schweitzer et al., 1996, Soc. Neurosci., abstract). Thus, according to current neurobiological models, the nucleus accumbens, amygdala, basal forebrain, and VT are central components of circuitry mediating brain processes underlying reward and memory of

that reward.

A number of human studies using cocaine infusions (Fowler et al., 1989; London et al., 1990; Pearlson et al., 1993; Volkow et al., 1997a) and withdrawing subjects (Volkow et al., 1990, 1991, 1992, 1993, 1997b) have implicated the striatum in human cocaine use, withdrawal, and craving. Given the spatial resolution of the techniques utilized, they may not have fully distinguished the dorsal and ventral striatum, in particular, the nucleus accumbens. None of these studies reported specific sampling of other regions implicated with reward processes, such as the VT, basal forebrain, or amygdala. Only three of these studies approached the 1–2 min temporal resolution needed to resolve components of cocaine-induced euphoria (Fowler et al., 1989; Pearlson et al., 1993; Volkow et al., 1997a).

Another learning suggests that [9]when heroin, oxycodone, or any other opiate travels through the bloodstream to the brain, the chemicals attach to specialized proteins, called mu opioid receptors, on the surfaces of opiate-sensitive neurons (brain cells). The linkage of these chemicals with the receptors triggers the same biochemical brain processes that reward people with feelings of pleasure when they engage in activities that promote basic life functions, such as eating and sex. Opioids are prescribed therapeutically to relieve pain, but when opioids activate these reward processes in the absence of significant pain, they can motivate the repeated use of the drug simply for pleasure.

One of the brain circuits that is activated by opioids is the mesolimbic (midbrain) reward system. This system generates signals in a part of the brain called the ventral tegmental area (VTA) that result in the release of the chemical dopamine (DA) in another part of the brain, the nucleus accumbens (NAc).This release of DA into the NAc causes feelings of pleasure. Other areas of the brain create a lasting record or memory that associates these good feelings with the circumstances and the environment in which they occur. These memories, called conditioned associations, often lead to the craving for drugs when the abuser re-encounters those persons, places, or things, and they drive abusers to seek out more drugs in spite of many obstacles.

Particularly in the early stages of abuse, the opioid's stimulation of the brain's reward system is a primary reason that some people take drugs repeatedly. However, the compulsion to use opioids builds over time to extend beyond a simple drive for pleasure. This increased compulsion is related to tolerance and dependence.

Opioid dependence and some of the most distressing opioid withdrawal symptoms stem from changes in another important brain system, involving an area at the base of the brain—the locus ceruleus (LC) (Neurons in the LC produce a chemical, noradrenaline (NA), and distribute it to other parts of the brain where it stimulates wakefulness, breathing, blood pressure, and general alertness, among other functions. When opioid molecules link to mu receptors on brain cells in the LC, they suppress the neurons' release of NA, resulting in drowsiness, slowed respiration, low blood pressure-familiar effects of opioid intoxication. With repeated exposure to opioids, however, the LC neurons adjust by increasing their level of activity. Now, when opioids are present, their suppressive impact is offset by this heightened activity, with the result that roughly normal amounts of NA are released and the patient feels more or less normal. When opioids are not present to suppress the LC brain cells' enhanced activity, however, the neurons release excessive amounts of NA, triggering jitters, anxiety, muscle cramps, and diarrhea.

[10]Drug cessation in the opioid-dependent state invariably elicits the opposite physiological and psychological manifestations from the acute drug state, resulting in physical withdrawal and the genesis of negative effect. Thus, opioid drugs such as morphine or oxycodone when given acutely induce euphoria and a sense of well being. Opioids also reduce stress hormone secretion and are known to be effective anxiolytics and anti-depressants when given acutely-Indeed, buprenorphine reduces depression severity scores in patients with treatment-resistant depression .In contrast to the acute drug effects, drug cessation from the opioid-dependent state induces agitation/panic attacks and dysphoria. Some drug-dependent people can tolerate the autonomic, hyperalgesic, anxiogenic, and/or effective components of withdrawal, whilst other individuals find it an almost insurmountable barrier, dreading withdrawal or having uncontrollable craving for relief from the withdrawal state (see discussion below). There are individual differences both in the initial propensity to take drugs and in the propensity to develop addictive behaviors. Following drug cessation, some individuals may never develop drug cravings, whilst others may retain a strong propensity to seek the drug state and exhibit addictive behaviors, especially following drug-associated triggers or cues. For example, many patients on opioid pain medications, though very much drug dependent, will go through withdrawal on drug cessation but never display addictive behaviors that are detrimental to their well-being. This is possibly due to pain patients having a learned association with pain relief (negative reinforcement). However, chronic pain patients with high catastrophizing scores are at risk of opioid misuse, as catastrophizing is

associated with craving in patients prescribed opioid analgesics (a strong determinant for opioid misuse) Similarly, impulsivity facets and distress intolerance (the perceived or actual inability to manage negative emotional and somatic states) were also identified to be a risk factor of prescription opioid misuse in the context of chronic pain treatment. Though tolerance and withdrawal symptoms have been retained in the revised Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM V) definition for substance use disorder, they are not stand-alone diagnostic criteria for this disorder.

[11]In general, rush experiences involved physical sensations of elevated heart rate and sweating, along with internal feelings variously characterized as "speeding" sensations and sensations of "being out of control". In contrast, the high experience was generally associated with feelings of self-confidence, well-being, and sociability. The low experience encompassed all negative subjective feelings potentially associated with cocaine use, such as anxiety, paranoia, dysphoria, or anhedonia.

[12]Given that chronic pain patients experience significant rates of suicidal ideation and suicide attempts, access to prescription opioids compounds the risk of death by suicide. These patients may experience heightened opioid craving and exhibit increased cue-reactivity to stimuli associated with past opioid use when suicidal ideation produces negative affective states. Because both opioids and suicidal behavior are used to alleviate emotional and physical pain through a process of negative reinforcement, elucidating factors that mediate this association may yield insight into suicide risk among chronic pain patients.

Treatment Implications

[13]Clinical trials to assess the effectiveness of medications or of behavioral interventions should be based on the conceptualization of addiction as a chronic disease (McLel- Lan et al., 2000). As for patients with other chronic diseases, most addicted subjects will require some type of continued therapeutic support (McLellan et al., 2005).

The evolving view of the neurobiological basis of the effects of substance abuse on the brain is continuously expanding the list of potential targets for intervention. The following medications are good examples of effective or promising treatments that emerged from a better understanding of the molecular and physiological bases of the reward, craving, withdrawal, and relapse phases of addiction.

Methadone

[14]Methadone is a long-acting opioid medication. Unlike morphine, heroin, oxycodone, and other addictive opioids that remain in the brain and body for only a short time, methadone has effects that last for days. Methadone causes dependence, but—because of its steadier influence on the mu opioid receptors—it produces minimal tolerance and alleviates craving and compulsive drug use. In addition, methadone therapy tends to normalize many aspects of the hormonal disruptions found in addicted individuals (Kling et al., 2000; Kreek, 2000; Schluger et al., 2001). For example, it moderates the exaggerated cortisol stress response that increases the danger of relapse in stressful situations.

Methadone treatment reduces relapse rates, facilitates behavioral therapy, and enables patients to concentrate on life tasks such as maintaining relationships and holding jobs. Pioneering studies by Dole, Nyswander, and Kreek in 1964 to 1966 established methadone's efficacy (Dole et al., 1966). As a Drug Enforcement Administration schedule II controlled substance, the medication is administered primarily in federally regulated methadone programs, where careful monitoring of patients' urine and regular drug counseling are critical components of rehabilitation. Patients are generally started on a daily dose of 20 mg to 30 mg, with increases of 5 mg to 10 mg until a dose of 60 mg to 100 mg per day is achieved. The higher doses produce full suppression of opioid craving and, consequently, opioid-free urine tests (Judd et al., 1998). Patients generally stay on methadone for 6 months to 3 years, some much longer. Relapse is common among patients who discontinue methadone after only 2 years or less, and many patients have benefited from lifelong methadone maintenance.

Buprenorphine

[15]Buprenorphine is a medication used to treat opioid addiction. A properly prescribed dose of buprenorphine can help opioid-addicted individuals to stop misusing opioids without experiencing withdrawal symptoms. Although buprenorphine is itself an opioid, and can thus have the same effects as other opioids (e.g., heroin, oxycodone), its maximum effects are less than those of other opioids.Therefore, with buprenorphine, there is a decreased risk of abuse, addiction, and side effects as compared with other opioids. Buprenorphine was approved for use in the United States for the treatment of opioid dependence in 2002 and is primarily available in two formulations: one that contains only buprenorphine (Subutex®) and one that contains buprenorphine and naloxone (Suboxone®).Naloxone reverses opioid overdoses and

prevents buprenorphine from being misused by injection. Most of the buprenorphine used for treatment in the United States is the buprenorphine-naloxone formulation, which can be prescribed by certified physicians. Availability of buprenorphine is less restricted than other treatments for opioid dependence, such as methadone, which can only be administered in specialized clinics. Although this availability can increase access to treatment, it can also increase the potential for diversion and misuse by those who are not opioid dependent. Such use can lead to buprenorphine dependence or abuse.

Harmful consequences can occur even when buprenorphine is taken as prescribed by a physician. If used by an individual who is dependent on large doses of opioids, buprenorphine can block the effect of other opioids and bring on withdrawal symptoms. Although these symptoms are not usually severe, emergency medical care may be required to relieve symptoms. Additionally, adverse reactions or drug interactions may occur.The potential for these consequences coupled with increasing availability call for careful monitoring of buprenorphine-related emergency department (ED) visits.

Modafinil

[16]Modafinil, a novel medication for the treatment of narcolepsy, is also being tested as a potential treatment for cocaine and methamphetamine dependence. Though the mechanism of action of modafinil is not properly understood, it is believed that it has both dopaminergic as well as glutamatergic effects. Hence, it has been proposed that modafinil could help counteract the cocaine-induced neuro-adaptations on DA and glutamate reward circuits that, in turn, could help alleviate cocaine withdrawal symptoms (Dackis et al., 2003).

[17]Modafinil has been regarded as a potential treatment for cocaine dependence for over 15 years, based on its dopaminergic and glutamatergic effects (Dackis et al., 2003). Early studies showed that modafinil could increase the rate of cocaine-free urine screens (Dackis et al., 2005) and reduce laboratory cocaine self-administration (Hart et al., 2008) in persons with cocaine dependence. Since then, outpatient, abstinence initiation treatment studies have cast doubt on its efficacy by not finding statistically significant main effects (e.g., Schmitz et al., 2012). However, secondary and post-hoc analyses in the two larger studies (Anderson et al., 2009; Dackis et al., 2012) showed evidence for positive effects on cocaine use measures like the maximum number of consecutive days of abstinence achieved and rates of cocaine-free urine screens. Recently, an outpatient trial in cocaine users without alcohol dependence

confirmed these findings, finding positive effects of modafinil on clinical outcomes (Kampman et al., 2015).

A potential concern with modafinil as a treatment for cocaine dependence is abuse liability. However, despite evidence that modafinil shows reinforcing effects when given to humans in a laboratory setting (Stoops et al., 2005), and has alerting effects similar to d-amphetamine (Makris et al., 2007), subjective drug effects from modafinil (e.g., similarity to amphetamine) are not consistently observed (Jasinski, 2000). Furthermore, although modafinil, like cocaine, is a dopamine transporter (DAT) blocker, it binds differently, less potently, less efficaciously, and for a longer duration to the DAT than does cocaine (Loland et al., 2012). These factors, along with its slow onset of action and formulation that is resistant to alteration and parenteral use, are likely why modafinil appears to have a low propensity for abuse. Notably, there are only rare case reports of dependence in locations where it is available over the counter and used widely as a "lifestyle" drug (e.g., Kate et al., 2012).

Topiramate

Topiramate (TPM; 2,3,4,5-bis-*O*-(1-methylethylidene)- *b*-D-fructopyranosesulfamate) is an *O*-alkyl sulfamate derivative of the naturally occurring monosaccharide D-fructose that showed efficacy in epilepsy Recently, TPM has been reported to be effective also in drug resistance partial epilepsy, refractory partial and secondary generalized seizures, primary generalized tonic/clonic seizures and tonic/atonic seizures associated with Lennox- Gastaut syndrome and may also improve myoclonic movements. Although in elderly patients with epilepsy TPM does not represent the first choice, it may be used in cognitively healthy elderly patients, for both high safety and low drug-drug interactions respect to other antiepileptic drugs. Preliminary data suggested that, in addition to its use in epilepsy, TPM may have therapeutic effects also in other neurological disorders and in psychiatric conditions, since other studies are needed to confirm these preliminary findings. The efficacy of TPM in bipolar and schizoaffective disorders, bulimia, neuropathic pain syndrome, migraine and cluster headache prophylaxis has been reported.Moreover, recently reviewing the literature about the use of TPM in hyperkinetic movement disorders, we described that the effectiveness of this drug is still inadequate and conclusive evidence has not been published.Finally, TPM seems to play a role in the treatment of cocaine addiction, gambling relapse, compulsive eating and sexual behavior. However, the clinical efficacy of topiramate

is associated with regular cognitive-behavioral therapy, suggesting that a combined effort can be used to improve psychiatric symptoms.

TPM facilitating gamma-aminobutyric acid (GABA) transmission and inhibiting glutamatergic transmission *via* AMPA/kainate receptors decreases the dopamine release in the cortico-mesolimbic system, that is involved in mechanisms of reward and reinforcement.Secondly, TPM blocks AMPA-type glutamate receptors in the nucleus paragigantocellularis through the inhibition of noradrenergic neurons in the locus coeruleus, the activation of which seems to be involved in the development of autonomic symptoms of withdrawal. Finally, TPM is a carbonic anhydrase inhibitor; this effect is involved in its anticonvulsant effects and could be important in the management of withdrawal.

TPM is used on-label in patients with epilepsy or a migraine. Main TPM targets include enhancement of GABAergic inhibition and reduction of AMPA receptors activity [3] that are involved in neuronal excitability control. Therefore TPM stabilizes neurons and decreases mesocorticolimbic dopamine release and could represent a potential candidate in cocaine-dependence treatment. In fact, attenuating the midbrain dopamine release, TPM could reduce the reinforcing and rewarding activities of drug abuse, and because it is a non-addictive agent, could be a more desirable alternative to other agents with abuse liability. Moreover, TPM may be used in several psychiatric disorders (*e.g.* obsessive-compulsive disorder, trichotillomania, bulimia nervosa, binge-eating disorder, and pathologic gambling).These psychiatric diseases show some similarities with drug-dependence, *i.e.* repetitive behaviors persisting minimal self-control despite significant negative consequences. TPM may be effective in these clinical conditions because it is able to reduce the reinforcing properties of these compulsive behaviors.

In the future, TPM could represent a therapeutic option in the management of cocaine dependence.

However, to date, there are only a few clinical studies regarding its role in cocaine users. Data from these clinical studies showed that the efficacy of TPM in cocaine treatment is often limited by a total number of subjects that was relatively small and by the number of participants who did not complete treatment. Despite its weaknesses, the results of these trial suggest that TPM may be beneficial for the treatment of comorbid cocaine (*i.e.* reducing anxiolytic and euphoric effects).

A recent Cochrane review of 20 studies with 2068 participants, regarding the efficacy and safety of anticonvulsant drugs for cocaine dependence, reported no conclusive significant evidence for use of TPM in the management of cocaine addiction.Probably due to the number of participants who did not complete treatment.

Social support groups as therapy for dependence

[19]Peer support can be defined as the process of giving and receiving non-professional, non-clinical assistance from individuals with similar conditions or circumstances to achieve long-term recovery from psychiatric, alcohol, and/or other drug-related problems. Historically, peer support has been shown to be a key component of much existing addiction treatments and recovery approaches such as the community reinforcement approach, therapeutic communities, and 12-step programs; the community reinforcement approach has demonstrated the importance of valued social roles in maintaining abstinence, which is the foundation of the peer support relationship.

Varying approaches that include a mixture of services such as peer support groups, individual counseling, and case management have emerged as a highly effective and empowering method to manage the social context of health issues and are particularly popular in the substance abuse and mental health fields. As it relates to substance abuse recovery for individuals and families, addiction peers support services have emerged across time due to the shift from a bio-psychosocial approach to a sustained recovery management approach to treat addictions. While in many cases, peer support groups do not replace the need for formal treatments or supervisory clinical guidance due to peers not having sufficient training to manage psychiatric conditions or high-risk situations, they still offer an augmentation to treatment that provides many benefits to individuals with substance use disorders.

Some of the most popular peer support groups held outside the formal treatment settings for addiction nationwide include 12-step programs such as AA, Narcotics Anonymous, and Cocaine Anonymous. Twelve-step is an intervention for drug abuse and addiction and can include dual recovery from substance abuse problems and co-occurring mental health disorders. Humphreys found 12-step groups to be the most referred adjunct support for professionally treated substance abuse patients. Other studies have demonstrated the effectiveness of 12-step groups for the treatment of substance abuse following treatment, and prior research of 12-step groups has shown reductions in alcohol and drug use.

AA has been shown to be a highly utilized intervention for individuals with alcohol problems. Positive outcomes such as self-efficacy and healthy coping have been associated with AA affiliation, which has been linked to better outcomes. For those with drinking problems seen in treatment, certain AA activities such as having a sponsor and doing service might be key components of abstinence.

In a focused review of the literature on AA effectiveness, six criteria were required for establishing causation: 1) magnitude of the effect; 2) dose-response effect; 3) consistent effect; 4) temporally accurate effects; 5) specific effects, and 6) plausibility. The evidence for all criteria except specific effects was very strong. For magnitude, rates of abstinence within AA were approximately twice as high. For dose–response, higher rates of abstinence were related to higher levels of attendance. For consistency, the effects were found for different follow-up periods and different samples. For temporal, prior AA attendance is predictive of subsequent abstinence. For plausibility, mechanisms of action predicted by behavioral change theories were present in AA. However, for the specificity of an effect for 12-step facilitation or AA, experimental evidence was mixed, with evidence for both positive and negative effects in addition to no effect.

Although the peer support groups within 12-step approaches have provided benefits to select populations, some individuals with substance use disorders find the religious nature of 12-step approaches and often lack of integration in the treatment setting to be a deterrent. Alternatives to 12-step approaches are needed to more closely integrate peer support services within treatment and to provide more options to benefit from peer support groups.

[20]Those who have participated in treatments, including peer support groups, have shown higher rates of abstinence than common in substance-abusing populations while also being more satisfied with the treatment. Furthermore, significant reductions in relapse rates were shown in addition to significant reductions in return to homelessness in a challenging population to treat. Reported benefits extended beyond those being the recipient of the peer support groups to those also delivering the services, where significant reductions in alcohol and drug use were shown not only for mentees but also for sustained abstinence in the majority of mentors.

CONCLUSION

Drug dependence and addiction are most appropriately understood as chronic medical disorders, like hypertension, schizophrenia, and diabetes. It is an alarming health hazard and social issue. Like some other diseases, a cure for drug addiction is unlikely, and frequent recurrences can be expected. Drug treatment over a long-term can limit the disease's adverse effects. It has been proven that acute pain management is a challenge in opioid-dependent patients as they are often undertreated for pain.In acute pain management in these patients, an appropriate opioid with an appropriate dosage should, therefore, be given to them to control the pain and prevent the development of withdrawal symptoms. Various pharmacotherapies like Methadone, Modafinil, Topiramate are examples of effective or promising treatments that have to a degree given positive results in a controlled and fixed dose.Overdose and misuse of these can also lead to abuse. With careful management, treatment for opioid dependence can be safe and more accessible than other forms of treatment.Other non-therapeutic treatments like therapy and support groups along with drug treatments are encouraged and have shown a positive outcome.

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