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# Addiction Research and Treatment

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The nation's leading causes of death are related to alcohol and drug use, tobacco smoke exposure, and behavioral addictions. Each year, more than 400,000 Americans die as a result of smoking, overeating, substance use, and related accidents and suicide. In addition, the comorbidity of addictions and psychiatric illnesses (ie, dual diagnosis) is quite common. Approximately 29% of those with a psychiatric disorder and almost half of those with severe mental illness (eg, schizophrenia) have a lifetime history of addiction.[1] As a result, addiction-related prevention, research, and treatment have remained important areas of concentration in the field of psychiatry.

There are significant individual differences in drug experimentation, drug(s) of choice, susceptibility to addiction, prognosis following intervention, and likelihood of relapse. Over the past few decades, there have been notable advances in the identification, prevention, and treatment of addiction disorders. For example, it was not until DSM-III-R that cocaine was listed as a potential substance of abuse, but this discovery expanded the focus of addiction research and treatment beyond specific physical withdrawal symptoms. More recently, animal models have improved and research is currently under way with addicted rats.[2] In addition, advances in neurobiology and imaging, proteomics, nanotechnology, pharmacology, and behavioral research have impacted the addiction field. This article highlights many of the latest developments in addiction research and focuses on those with a clear application to psychiatric practice.

**Influence of neurobiology and neurotransmitters**

Several components of the neurological reward system (eg, the nucleus accumbens, the ventral tegmental area, and the neurotransmitters [particularly dopamine]) have been implicated in addiction. For example, release of dopamine in the nucleus accumbens is associated with craving for cocaine and drug-seeking behavior.[3,4] Similarly, morphine, cannabis, nicotine, and ethanol administration result in increased dopamine release in the nucleus accumbens.[5-7] They are also associated with molecular adaptations in dopamine transporters, as well as opioid, g-aminobutyric acid (GABA), and nicotinic cholinergic receptors throughout the brain.[8-10] In addition, the brain's endogenous opioid and cannabinoid systems, within the pathway connecting the ventral tegmental area and the nucleus accumbens, are activated by several drugs of abuse.[11] Increased glutamate release in the pathway connecting the prelimbic cortex to the accumbens is associated with drug-seeking behavior.[12] With

regard to tobacco, findings from recent research indicate that patients with damage to the insula (an area associated with consciously experiencing an urge) were able to immediately quit smoking, without the typical urges and relapses that usually characterize smoking cessation.[13]

Research findings indicate that individual differences in sensitivity to substances of abuse may be affected by genetic factors and early environmental factors, and strong interactions between the cannabinoid and opioid systems within the brain may produce cross-sensitization of neurons following exposure to substances of abuse.[14,15] Several pharmacological interventions for the treatment of addiction and the prevention of relapse target these neurotransmitters and their receptors.

When considering the possibility that all addictions represent 1 disease, one would expect a common neurobiology, as well as transposable treatments that might work for multiple addictions. For example, naltrexone was used in the 1970s for opioid relapse prevention and has been subsequently used to treat alcohol dependence, gambling, compulsive eating, and other addictions. Drug self-administration represents an acquired drive that results in use despite pain and suffering; it appears to be caused, in part, by pathological learning and preoccupation with the substance. This may help to explain the mechanisms of action in complete blockers such as naltrexone, partial agonists such as buprenorphine, and agonists such as methadone. Research continues to identify brain events associated with pleasure, which may shape behavior and the development of addiction.

**Imaging studies**

Neuroimaging with MRI, magnetic resonance spectroscopy, positron emission tomography (PET), single photon emission CT (SPECT), and functional MRI scanning has helped to confirm that addiction is a disease marked by changes in brain structure and functioning, as well as behavioral correlates. In their review of the literature, Fowler and colleagues[16] noted that structural abnormalities in the frontal cortex, prefrontal cortex, basal ganglia, and amygdala have been associated with abuse of various substances. Similarly, they reviewed functional imaging studies, which have demonstrated that the caudate nucleus, cingulate, and prefrontal cortex become activated during a drug "rush," whereas the nucleus accumbens becomes activated during periods of craving. PET and SPECT studies have highlighted the role of striatal dopamine in drug-related reward and addiction.

The dopamine spike that causes the pleasurable drug-related "high" is believed to attenuate drug users' ability to experience pleasure in other activities.[9] In addition, findings from recent studies indicate that drug effects are long-lasting and recovery is slow and difficult. Imaging may also be useful in determining the likelihood of relapse in patients, which may have implications for treatment recommendations.[17]

**Developmental neurobiology**

Risk factors for alcohol dependence have been well studied, and many scientists expect that genes for alcoholism risk will be identified in the near future. However, early alcohol exposure and binge drinking appear to play a critical role in the development of alcohol dependence. Similarly, early brain exposure to drugs of abuse (whether in utero or through secondhand exposure) may sensitize the brain, making abuse and dependence more likely. For example, parents who drink alcohol inadvertently teach their children to identify the smell of their favorite alcoholic beverage. Mothers who smoke frequently have children who smoke, which may be associated with early secondhand smoke exposure.

In an animal model, rats that were exposed to tetrahydrocannabinol during adolescence showed higher levels of opioid self-administration during adulthood than rats that had not been exposed.[18] In humans,

correlational twin studies have shown that regular use of marijuana during adolescence is associated with use of other illicit drugs in the future.[19,20]

Drugs of abuse cause specific interactions within the brain's most primitive and salience-provoking systems. They change the brain and can produce disease where none would have been without early use or exposure. Although the "gateway hypothesis" describes the progression from tobacco/marijuana use in adolescence to later abuse of "hard" drugs via attitude changes, it is possible that the earlier tobacco or marijuana use actually sensitizes the brain, making it remember the effects of drug use, and making it more susceptible to abuse of other drugs in the future. Indeed, preliminary research shows that anesthesiologists who experience long-term secondhand exposure to extremely low doses of opioids in the air of the operating room are at increased risk for opioid addiction.[21] Furthermore, persons with a history of smoking marijuana or tobacco appear to be at highest risk.[22]

More research is needed to explore these hypotheses and determine the mechanism(s) involved. Until then, it may be safest to address patients' substance use/abuse (even with soft drugs such as marijuana) as early as possible. This approach is relatively inexpensive and could potentially decrease the likelihood of a long-term addiction developing without increasing risk to the patient.

**Proteomics research**

Recently, methods of proteomics and genomics have been applied to the study of molecular mechanisms and neurobiological consequences of drug administration. Using animal models, advances in the understanding of neural circuitry and cellular mechanisms involved in addiction have paved the way for improved understanding of addiction in humans and may eventually provide information needed to develop more effective prevention and treatment methods. Nestler[23] has demonstrated that drug addiction is associated with changes at the molecular level, which may be understood as a form of neural plasticity that results from long-term drug use.

Kobeissy and colleagues[24] reviewed the existing animal and human proteomic research on the cellular effects of morphine, methamphetamine, and alcohol, particularly in the prefrontal cortex, striatum, and hippocampus. They reported that morphine administration is associated with dysregulation of proteins involved with several crucial cellular functions (eg, metabolism, signal transduction, organization of the cytoskeleton, synaptic transmission). Similarly, acute methamphetamine administration appears to negatively alter cellular functioning in many ways (eg, oxidative stress, synaptic transmission, mitochondrial dysfunction, apoptosis). It is noteworthy that data assessing the impact of chronic alcohol administration demonstrate similar dysfunction in signaling and cytoskeleton organization, as well as increased oxidative stress. These data suggest that drug abuse may result in permanent damage to cellular structure and functioning, even in the absence of behavioral markers. Current proteomic studies are assessing inflammatory response and damage caused by drugs (eg, methamphetamine) and evaluating the length of time before brain functioning "recovers" following a drug binge.[25,26]

**Stress and relapse**

It is generally understood that among patients with addiction disorders, relapse is the rule rather than the exception. Drug dependence appears to be related to dysregulation of the reward system and withdrawal-related activation of the stress system.[27] Stress hormones (eg, corticosterone, prolactin) increase in response to withdrawal from psychoactive drugs, increasing the aversive quality of the experience.[28]

Factors associated with classical and operant conditioning and social learning produce environmental and behavioral "cues" that may increase urges and encourage use. As a result, treatment efforts typically involve relapse prevention techniques that help individuals prepare for recovery by assessing personal antecedents of relapse and adjusting expectations.[29] Psychoeducation, self-efficacy support, and coping skills training are important components of the intervention. The patient and clinician work together to identify situations associated with a high-risk for substance use and ways to avoid or minimize exposure to these situations. The clinician also helps the patient learn ways to manage urges, cravings, and withdrawal symptoms.

**Pharmacotherapy**

Building on the findings related to neurobiological influences in addiction and the importance of managing relapse, investigators have developed several pharmacological interventions to manage the symptoms of intoxication and withdrawal, as well as to control cravings. For example, the introduction of naloxone, an opioid antagonist, as an emergency intervention for narcotic overdose has saved countless lives.[30]

The next major advance occurred when clonidine (an a2-adrenergic agonist) was identified as a nonopiate treatment to reverse the effects of opiate withdrawal.[31] Building on this finding, treatment with naltrexone (a pure opioid antagonist) following clonidine therapy was introduced to assist with rapid drug detoxification and to offer an alternative to methadone maintenance therapy.[32] Methadone maintenance therapy and buprenorphine therapy continue to assist individuals in managing symptoms of withdrawal to overcome opiate addiction; however, the advances in detoxification methods allow individuals the opportunity to live drug free.

More recently, injectable naltrexone has been approved to help individuals who struggle with adherence to daily treatment. In addition, acamprosate (a GABA agonist/glutamate antagonist) has been shown to be efficacious in reducing alcohol consumption in persons with alcohol dependence, without adverse effects.[33] However, in a recent study, naltrexone and/or behavioral therapy were found to be more efficacious than treatment with acamprosate or placebo.[34] Varenicline, a partial nicotine agonist, has been approved to treat nicotine dependence by combating withdrawal symptoms and blocking the effects of nicotine. Unfortunately, no pharmacological treatments for cocaine yet exist, and prevention remains the best treatment.

**Behavioral treatments**

Many persons with substance abuse actually choose to change their behavior on their own.[35] However, for those who are not ready to change, motivational interviewing approaches may help.[36] Motivational interviewing is a brief, patient-centered, directive approach that emphasizes personal choice and responsibility. It has demonstrated efficacy with addiction populations related to both quitting/cutting down on substance use or accepting formal treatment. In addition, research has shown that contingency management techniques, most notably voucher-based reinforcement therapy, can help patients achieve abstinence from various substances of abuse including cocaine and other stimulants, opioids, marijuana, tobacco, and alcohol.[37] Voucher-based reinforcement therapy has also shown efficacy in promoting adherence to pharmacotherapy, psycho- therapy, and other support services

Cognitive-behavioral therapy (CBT) is a relatively brief treatment approach that often serves as the foundation of psychosocial intervention for patients with addictions. CBT typically combines psychoeducation, functional analysis, skill-building, environmental modification and contingency

management, examination of dysfunctional thinking, coping skills training, and other techniques. The therapist will teach and encourage more adaptive thinking, work with the patient to address barriers to sobriety, teach alternative coping strategies, and assist the patient to identify and elicit social support. Marital and/or family therapy may also be used to augment other interventions in order to decrease environmental conflict and improve support, because this is generally associated with greater success in maintaining recovery.[38]

**12-Step programs**

Participation in a 12-step program (eg, Alcoholics or Narcotics Anonymous, Double Trouble in Recovery) is beneficial for many individuals with an addiction disorder.39 Although some individuals are hesitant to join these groups, psychiatrists can assist these patients through "12-step facilitation."40 This approach involves providing psychoeducation and focusing on 3 core topics:

- Introducing the patient to the 12-step philosophy.
- Working with the patient to complete the first 3 steps.
- Encouraging the patient to become actively involved in a 12-step program.

Alcoholics Anonymous is currently the most popular mutual-help group for Americans with alcohol addiction, but even those with dual diagnosis benefit from participation in a 12-step program.[41] Indeed, participation in a 12-step program is associated with increased self-efficacy for abstinence and spirituality.[42] Participants who help others show lower rates of relapse, and most participants in the later stages of recovery continue to help other addicts.[42,43]

**Drug testing**

Research and clinical experience also demonstrate the utility of random drug testing as both a preventive tool and a component of treatment for patients with chemical addictions. Although many clinicians rely on self-reports or collateral reports, because of improved accuracy, urine screening is generally viewed as the preferred method for assessing substance use.[44] It is also more sensitive and less invasive than blood testing, and it can be augmented by hair testing (for some drugs) to assess for drug use over long periods. Negative findings on drug testing are a common outcome measure in addiction research and an essential component of recovery according to the Betty Ford Institute Consensus Panel.[45] When alcohol is the drug of abuse, urine screening for ethyl glucuronide may provide a more sensitive assessment than blood or breath tests.[46] Drug testing does not provide information regarding levels of impairment or presence of an addiction; rather, results indicate whether the drug was recently used by the individual.

Several kits that do not require special training to administer are available for rapid testing in the office. Other tests can be sent out for laboratory analysis. Methods to decrease the likelihood of tampering with urine testing (eg, direct urethral supervision, point-of-care testing, and analysis for adulterants and unreliable samples) have been developed and are available as well.[47] Drug testing allows clinicians to identify more individuals with substance use disorders, who may otherwise have their disorders misdiagnosed. For example, within an emergency department, up to 45% of admissions are directly related to drug use, and the prevalence of substance-related admissions increases significantly when alcohol use is also considered.[48] As "drugged driving" becomes more problematic, and other substance-related visits continue, substance abuse clinicians will likely be enlisted to provide screening and brief interventions in the emergency department.

**Impaired-physician programs**

Although up to 90% of addicted persons in the general population experience relapse within 1 year, only 10% to 25% of physicians who attend specialized treatment programs share this outcome.[49-52] In addition, those who do relapse typically reenter recovery with booster treatment.[53] Various factors may contribute to their success, including high levels of resources (eg, intellectual, financial, social).

However, it is noteworthy that programs for impaired professionals provide the most comprehensive treatment available. They generally use psychoeducational sessions, individual CBT, group therapy, 12-step programs, relapse-prevention, family-based psychotherapy sessions, and contingency management. In addition, physicians generally spend more time in treatment and have access to more intensive/individualized care.[54] Follow-up services are more intensive and are characterized by random drug testing with immediate consequences for positive results. Many physicians in recovery cite continued urine testing as a powerful deterrent to drug use, which greatly increases their motivation to remain abstinent.

Although this comprehensive approach is very expensive, the success rate provides support for its implementation on a wider scale. When considering the actual cost of addiction (including health care costs, lost wages, legal fees, mortality risks), paying for high-quality intensive treatment may be a more cost-effective alternative.

**Public health interventions**

In addition to individual treatment programs, societal interventions can greatly influence drug use in the general population. For example, the implementation of indoor smoking bans significantly decreased rates of tobacco use and secondhand smoke exposure. Similarly, increased taxes on tobacco products serve as a successful prevention strategy, and increased alcohol taxes have been associated with significantly reduced alcohol-related mortality.[55,56]

Some research has demonstrated preliminary positive effects of television commercials produced by the Partnership for a Drug-Free America in reducing drug use among teenagers.[57] Whereas adolescents' self-reported substance use has shown a fairly stable decrease since 1996, deaths related to certain drugs appear to be increasing in some areas.[58-60] Reducing prescription misuse, illicit drug use, and their consequences remains a major challenge for our nation, and no long-term effective strategy has been identified. More research is needed to evaluate additional methods of public health prevention and intervention for addiction.

**Addiction as a unitary disease**

Although drugs of abuse are diverse and affect the brain via different acute mechanisms of action, each influences the reward circuitry of the brain's limbic system by increasing dopamine release in the nucleus accumbens. As suggested by Nestler,[61] it is possible that a common molecular pathway underlies all addictions, and perhaps this can be exploited to develop more effective treatments.

Applied research has shown that treatment outcomes for impaired physicians do not differ based on their choice of substance (R. L. DuPont et al, unpublished data, 2008); physicians with addiction to opioids or crack cocaine fare as well as those with alcohol dependence. Given the high prevalence of polysubstance abuse and the fact that the same treatment appears to be effective for alcohol, opioid, marijuana, benzodiazepine, and cocaine dependence, it may be more useful to consider the treatment of addiction disorders rather than attempt to tailor interventions based on a specific drug of abuse.

**Behavioral addictions**

Research is accumulating regarding the similarities among chemical addictions and other compulsive-behavior disorders.[62] For example, researchers have developed an animal model of food addiction (sugar) in rats that closely parallels that seen with drug addiction.[63] Imaging studies in humans also point to a shared neurobiological mechanism. Pathological gambling, hypersexual behavior, and compulsive eating are frequently comorbid with drug addiction and share similar neurological patterns.[64-66] In each case, alterations in the natural reward pathway appear to be implicated in the tendency to continue the behavior despite negative consequences. Although similar behavioral and pharmacological treatments have shown efficacy with these groups, more research is needed to clarify the process of addiction and determine how and why addiction manifests in various behaviors and substances of abuse. In the meantime, clinicians should be vigilant for signs of "addiction transfer" in patients who are attempting sobriety, because preliminary evidence suggests that these patients may be more vulnerable to symptoms of behavioral addiction and vice versa.[67]

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Addiction Research and Treatment Interviews. Experience 1 Rating. Experience.Â  Addiction Research and Treatment Awards & Accolades. Let us know if we're missing any workplace or industry recognition â€“ Add Awards. Work at Addiction Research and Treatment? Share Your Experiences. Addiction Research and Treatment. Star Very Dissatisfied. Star Dissatisfied. Addiction-related prevention, research, and treatment have remained important areas of concentration in the field of psychiatry.Â  The nation's leading causes of death are related to alcohol and drug use, tobacco smoke exposure, and behavioral addictions. Each year, more than 400,000 Americans die as a result of smoking, overeating, substance use, and related accidents and suicide. In addition, the comorbidity of addictions and psychiatric illnesses (ie, dual diagnosis) is quite common. Approximately 29% of those with a psychiatric disorder and almost half of those with severe mental illness (eg, schizophrenia) have a lifetime history of addiction.1 As a result, addiction-related prevention, research, and treatment h