Substance dependence

This article is about Drug and alcohol dependence. For alcohol dependence, see alcohol dependence. For the journal, see Drug and Alcohol Dependence (journal). For substance abuse, see substance abuse.

Substance dependence also known as **drug dependence** is an adaptive state that develops from repeated drug administration, and which results in withdrawal upon cessation of drug use.[1][2] A *drug addiction*, a distinct concept from substance dependence, is defined as compulsive, out-of-control drug use, despite negative consequences.[1][2] An *addictive drug* is a drug which is both rewarding and reinforcing.[1] ΔFosB, a gene transcription factor, is now known to be a critical component and common factor in the development of virtually all forms of behavioral addiction and drug addictions, but not dependence.[3][4][5]

Substance dependence	
Classification and external resources	
Specialty	Psychiatry
ICD-10	F10.2-F19.2
ICD-9-CM	303-304
MeSH	D019966

Within the framework of the 4th edition of the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM-IV*), substance dependence is redefined as a drug addiction, and can be diagnosed without the occurrence of a withdrawal syndrome.[6] It is now described accordingly: "When an individual persists in use of alcohol or other drugs despite problems related to use of the substance, substance dependence may be diagnosed. Compulsive and repetitive use may result in tolerance to the effect of the drug and withdrawal symptoms when use is reduced or stopped. This, along with Substance Abuse are considered Substance Use Disorders."[7]

Addiction and dependence glossary[8][9][10][11]

- **addiction** – a medical condition characterized by compulsive engagement in rewarding stimuli despite adverse consequences
- **addictive behavior** – a behavior that is both rewarding and reinforcing
- **addictive drug** – a drug that is both rewarding and reinforcing
- **dependence** – an adaptive state associated with a withdrawal syndrome upon cessation of repeated exposure to a stimulus (e.g., drug intake)
- **drug sensitization** or **reverse tolerance** – the escalating effect of a drug resulting from repeated administration at a given dose
- **drug withdrawal** – symptoms that occur upon cessation of repeated drug use
- **physical dependence** – dependence that involves persistent physical–somatic withdrawal symptoms (e.g., fatigue and delirium tremens)
- **psychological dependence** – dependence that involves emotional–motivational withdrawal symptoms (e.g.,

dysphoria and anhedonia)

• **reinforcing stimuli** – stimuli that increase the probability of repeating behaviors paired with them

• **rewarding stimuli** – stimuli that the brain interprets as intrinsically positive or as something to be approached

• **sensitization** – an amplified response to a stimulus resulting from repeated exposure to it

• **substance use disorder** - a condition in which the use of substances leads to clinically and functionally significant impairment or distress

• **tolerance** – the diminishing effect of a drug resulting from repeated administration at a given dose

Withdrawal

Main article: Drug withdrawal

Withdrawal is the body's reaction to abstaining from a substance upon which a person has developed a dependence syndrome. When dependence has developed, cessation of substance use produces an unpleasant state, which promotes continued drug use through negative reinforcement; i.e., the drug is used to escape or avoid re-entering the associated withdrawal state. The withdrawal state may include physical-somatic symptoms (physical dependence), emotional-motivational symptoms (psychological dependence), or both. Chemical and hormonal imbalances may arise if the substance is not introduced. Psychological stress may also result if the substance is not re-introduced.

Risk factors

Dependence potential

The dependence potential of a drug varies from substance to substance, and from individual to individual. Dose, frequency, pharmacokinetics of a particular substance, route of administration, and time are critical factors for developing a drug dependence.

An article in *The Lancet* compared the harm and dependence liability of 20 drugs, using a scale from zero to three for physical dependence, psychological dependence, and pleasure to create a mean score for dependence. Selected results can be seen in the chart below.[12]

Drug	Mean	Pleasure	Psychological dependence	Physical dependence
Heroin	3.00	3.0	3.0	3.0
Cocaine	2.39	3.0	2.8	1.3
Tobacco	2.21	2.3	2.6	1.8
Barbiturates	2.01	2.0	2.2	1.8
Alcohol	1.93	2.3	1.9	1.6
Benzodiazepines	1.83	1.7	2.1	1.8
Amphetamine	1.67	2.0	1.9	1.1
Cannabis	1.51	1.9	1.7	0.8
Ecstasy	1.13	1.5	1.2	0.7

Capture rates

Capture rates enumerate the percentage of users who reported that they had become dependent to their respective drug at some point.[13][14]

Drug	% of users
Cannabis	9%
Alcohol	15.4%
Cocaine	16.7%
Heroin	23.1%
Tobacco	31.9%

Biomolecular mechanisms

Psychological dependence

Two factors have been identified as playing pivotal roles in psychological dependence: the neuropeptide "corticotropin-releasing factor" (CRF) and the gene transcription factor "cAMP response element binding protein" (CREB).[8] The reward system is partly responsible for the psychological part of drug dependence. The CREB protein is activated by cyclic adenosine monophosphate (cAMP) immediately after a high and triggers changes in gene expression that affect proteins such as dynorphin, which cuts off dopamine release and temporarily inhibits the reward pathway. A sustained activation of CREB thus forces a larger dose to be taken to reach the same effect. In addition, it leaves the user feeling generally depressed and dissatisfied, and unable to find pleasure in previously enjoyable activities, often leading to a return to the drug for another dose.[15]

In addition to the reward pathway, it is hypothesized that stress mechanisms play a role in dependence. Boob and Kreek have hypothesized that during drug use, the corticotropin-releasing factor activates the hypothalamic-pituitary-adrenal axis (HPA) and other stress systems in the extended amygdala. This activation influences the dysregulated emotional state associated with psychological dependence. They have found that as drug use escalates, so does the presence of CRF in human cerebrospinal fluid (CSF). In rat models, the separate use of

CRF antagonists and CRF receptor antagonists both decreased self-administration of the drug of study. Other studies in this review showed a dysregulation in other hormones associated with the HPA axis, including enkephalin which is an endogenous opioid peptide that regulates pain. It also appears that the μ-opioid receptor system, which enkephalin acts on, is influential in the reward system and can regulate the expression of stress hormones.[16]

Diagnosis

DSM classification

"Substance dependence", as defined in the DSM, can be diagnosed with physiological dependence, evidence of tolerance or withdrawal, or without physiological dependence. DSM-5 substance dependencies include:

- 303.90 Alcohol dependence
- 304.00 Opioid dependence
- 304.10 Sedative, hypnotic, or anxiolytic dependence (including benzodiazepine dependence and barbiturate dependence)
- 304.20 Cocaine dependence
- 304.30 Cannabis dependence
- 304.40 Amphetamine dependence (or amphetamine-like)
- 304.50 Hallucinogen dependence
- 304.60 Inhalant dependence
- 304.80 Polysubstance dependence
- 304.90 Phencyclidine (or phencyclidine-like) dependence
- 304.90 Other (or unknown) substance dependence
- 305.10 Nicotine dependence

Management

Addiction is a complex but treatable condition. It is characterized by compulsive drug craving, seeking, and use that persists even if the user is aware of severe adverse consequences. For some people, addiction becomes chronic, with periodic relapses even after long periods of abstinence. As a chronic, relapsing disease, addiction may require continued treatments to increase the intervals between relapses and diminish their intensity. While some with substance issues recover and lead fulfilling lives, others require ongoing additional support. The ultimate goal of addiction treatment is to enable an individual to manage their substance misuse; for some this may mean abstinence. Immediate goals are often to reduce substance abuse, improve the patient's ability to function, and minimize the medical and social complications of substance abuse and their addiction; this is called "harm reduction".

Treatments for addiction vary widely according to the types of drugs involved, amount of drugs used, duration of the drug addiction, medical complications and the social needs of the individual. Determining the best type of recovery program for an addicted person depends on a number of factors, including: personality, drugs of choice, concept of spirituality or religion, mental or physical illness, and local availability and affordability of programs.

Many different ideas circulate regarding what is considered a successful outcome in the recovery from addiction. Programs that emphasize controlled drinking exist for alcohol addiction. Opiate replacement therapy has been a medical standard of treatment for opioid addiction for many years.

Treatments and attitudes toward addiction vary widely among different countries. In the US and developing countries, the goal of commissioners of treatment for drug dependence is generally total abstinence from all drugs. Other countries, particularly in Europe, argue the aims of treatment for drug dependence are more complex, with treatment aims including reduction in use to the point that drug use no longer interferes with normal activities such as work and family commitments; shifting the addict away from more dangerous routes of drug administration such as injecting to safer routes such as oral administration; reduction in crime committed by drug addicts; and treatment of other comorbid conditions such as AIDS, hepatitis and mental health disorders. These kinds of outcomes can be achieved without eliminating drug use completely. Drug treatment programs in Europe often report more favorable outcomes than those in the US because the criteria for measuring success are functional rather than abstinence-based.[17][18][19] The supporters of programs with total abstinence from drugs as a goal believe that enabling further drug use means prolonged drug use and risks an increase in addiction and complications from addiction.[20]

Residential

Residential drug treatment can be broadly divided into two camps: 12-step programs and therapeutic communities. Twelve-step programs are a nonclinical support-group and faith-based approach to treating addiction. Therapy typically involves the use of cognitive-behavioral therapy, an approach that looks at the relationship between thoughts, feelings and behaviors, addressing the root cause of maladaptive behavior. Cognitive-behavioral therapy treats addiction as a behavior rather than a disease, and so is subsequently curable, or rather, unlearnable. Cognitive-behavioral therapy programs recognize that, for some individuals, controlled use is a more realistic possibility.[21]

One of many recovery methods are 12-step recovery programs, with prominent examples including Alcoholics Anonymous, Narcotics Anonymous, Drug Addicts Anonymous[22] and Pills Anonymous. They are commonly known and used for a variety of addictions for the individual addicted and the family of the individual. Substance-abuse rehabilitation (rehab) centers offer a residential treatment program for some of the more seriously addicted, in order to isolate the patient from drugs and interactions with other users and dealers. Outpatient clinics usually offer a combination of individual counseling and group counseling. Frequently, a physician or psychiatrist will prescribe medications in order to help patients cope with the side effects of their addiction. Medications can help immensely with anxiety and insomnia, can treat underlying mental disorders (cf. self-medication hypothesis, Khantzian 1997) such as depression, and can help reduce or eliminate withdrawal symptomology when withdrawing from physiologically addictive drugs. Some examples are using benzodiazepines for alcohol detoxification, which prevents delirium tremens and complications; using a slow taper of benzodiazepines or a taper of phenobarbital, sometimes including another antiepileptic agent such as gabapentin, pregabalin, or valproate, for withdrawal from barbiturates or benzodiazepines; using drugs such as baclofen to reduce cravings and propensity for relapse amongst addicts to any drug, especially effective in stimulant users, and alcoholics (in which it is nearly as effective as benzodiazepines in preventing complications); using clonidine, an alpha-agonist, and loperamide for opioid detoxification, for first-time users or those who wish to attempt an abstinence-based recovery (90% of opioid users relapse to active addiction within eight months or are multiple relapse patients); or replacing an opioid that is interfering with or destructive to a user's life, such as illicitly-obtained heroin, dilaudid, or oxycodone, with an opioid that can be administered legally, reduces or eliminates drug cravings, and does not produce a high, such as methadone or buprenorphine – opioid replacement therapy – which is the gold standard for treatment of opioid dependence in developed countries, reducing the risk and cost to both user and society more effectively than any other treatment modality (for opioid dependence), and shows the best short-term and long-term gains for the user, with the greatest longevity, least risk of fatality, greatest quality of life, and lowest risk of relapse and legal issues including arrest and incarceration.

In a survey of treatment providers from three separate institutions, the National Association of Alcoholism and Drug Abuse Counselors, Rational Recovery Systems and the Society of Psychologists in Addictive Behaviors, measuring the treatment provider's responses on the "Spiritual Belief Scale" (a scale measuring belief in the four spiritual characteristics of AA identified by Ernest Kurtz); the scores were found to explain 41% of the variance in the treatment provider's responses on the "Addiction Belief Scale" (a scale measuring adherence to the disease model or the free-will model of addiction).[23]

Behavioral programming

Behavioral programming is considered critical in helping those with addictions achieve abstinence. From the applied behavior analysis literature and the behavioral psychology literature, several evidence based intervention programs have emerged: (1) behavioral marital therapy; (2) community reinforcement approach; (3) cue exposure therapy; and (4) contingency management strategies.[24][25] In addition, the same author suggest that Social skills training adjunctive to inpatient treatment of alcohol dependence is probably efficacious. Community reinforcement has both efficacy and effectiveness data.[26] In addition, behavioral treatment such as community reinforcement and family training (CRAFT) have helped family members to get their loved ones into treatment.[27][28] Motivational Intervention has also shown to be an effective treatment for substance dependence.

Alternative therapies

Alternative therapies, such as acupuncture, are used by some practitioners to alleviate the symptoms of drug addiction. In 1997, the American Medical Association (AMA) adopted as policy the following statement after a report on a number of alternative therapies including acupuncture:

> There is little evidence to confirm the safety or efficacy of most alternative therapies. Much of the information currently known about these therapies makes it clear that many have not been shown to be efficacious. Well-designed, stringently controlled research should be done to evaluate the efficacy of alternative therapies.[29]

Acupuncture has been shown to be no more effective than control treatments in the treatment of opiate dependence.[30] Acupuncture, acupressure, laser therapy and electrostimulation have no demonstrated efficacy for smoking cessation.[31]

Important phases in treating substance dependence include establishing coping mechanisms to deal with the hardships of withdrawal symptoms. With the correct approaches, the patient can live a healthier life.[32]

Online websites have been a resource to aid in helping people to overcome addictions. These websites act as ways for struggling addicts, family members of addicts, and people who are in the recovery stage to confide in each other (anonymously if they so choose). They provide an alternative way for these people to seek help, support and information. Sites typically include chat rooms, forums, and blogs for members to interact.

Treatment and Issues

Psychologists need to use many techniques and approaches to implement the right application to fix substance related disorders. Psychodynamic approach is one of the techniques that psychologist use to solve the addictions problems. In the Psychodynamic therapy, psychologists need to understand the conflicts and the needs of the

addict persons, and also need to locate the defects of their ego and defense mechanisms. Using this approach alone by itself is proved to be ineffective in solving addiction problems. Psychology is not only defined by conscious as believed in structuralism ideology, is also defined by cognition and behavior. Therefore, cognitive and behavioral techniques should be integrated with psychodynamic approaches to achieve effective treatment to substance related disorders (Comer, 2013; Cornish et al., 1995; Lightdale et al., 2011, 2008). Cognitive treatment required psychologist to think deep in what is happening in the brain of addict persons. Cognitive psychologists should zoom in to neural functions of the brain and understand that drugs have been manipulating the dopamine rewarding center of the brain. To put it in other words, Drugs have become the only rewarding pleasurable resource of daily life. From this particular state of thinking Cognitive psychologist need to find ways to change the thought process of addict persons (Comer, 2013; de Wit and Phan, 2010).

There are two routes that should be applied to cognitively fix substance abuse persons; track the thoughts that pulled them to addictions and track the thoughts that prevent them from relapsing. Nevertheless, psychologist should also add the principle of functionalism in the equation of treating substance related disorder. As matter of fact behavioral techniques have the largest wide share of application in treating substance related disorders. Behavioral psychologists would use the techniques of “aversion therapy”. This sort of therapy is based on the principles of classical conditioning of Ivan Pavlov. It is when pairing substance abuse with unpleasant stimulus or condition, for example, pairing pain, electrical shock, or nausea with alcohol consumption. The latter required using some nausea-induced medications (Comer, 2013; Owen-Howard, 2010; Welsh & Liberto, 2001). Therefore, it is better for psychologists to use an integration of all these approaches to produce reliable and effective treatment. With advanced clinical use of medications, biological treatment has considered to be one of the efficient interventions that psychologists may use as a short cut treatment for addict persons. Biological interventions involved many approaches; one approach is to reduce regularly the dosages intake of the harmful substances.

The other approach is to use medicines that contain chemicals that interfere with the functions of the drugs in the brain. The third approach is when substituting addiction drugs with other addiction drugs. The next paragraph would explain how this approach is problematic and involve in the debate of ethical concerns. Those three conditions of biological interventions have aimed on the process of detoxification within the substance abuse individuals, especially the ones whose drugs become the center of their life. Psychologists need to think of the consequences when understanding how the process of detoxification is a difficult stage and might throw individuals with addiction problems into unpleasant conditions and painful experience. Moreover, Psychologist needs to realize that by using biological interventions they are purposely and intentionally throwing drug abusive people into unwanted withdrawal symptoms. This might inflict pain and dangerous consequences on the addict persons. Therefore, biological intervention should be combined with Humanistic approaches and other therapeutic techniques. Self- Help therapies is a group therapy technique which include anonymity, teamwork and sharing concerns of daily life among people who suffer from addiction issues. However, these programs proved to be only effective and influential on persons who did not reach the level of serious dependency on drugs or alcohol. Self-help therapy proved to be effective on young people who have self-conscious about their problems (Comer, 2013).

History

The phenomenon of drug addiction has occurred to some degree throughout recorded history (see "Opium").[33] Modern agricultural practices, improvements in access to drugs, advancements in biochemistry, and dramatic increases in the recommendation of drug usage by clinical practitioners have exacerbated the problem significantly in the 20th century. Improved means of active biological agent manufacture and the introduction of synthetic compounds, such as methamphetamine, are also factors contributing to drug addiction.[34][35]

For the entirety of US history, drugs have been used by some members of the population. In the country's early years, most drug use by the settlers was of alcohol or tobacco.[36]

The nineteenth century saw opium usage in the US become much more common and popular. Morphine was isolated in the early nineteenth century, and came to be prescribed commonly by doctors, both as a painkiller and as an intended cure for opium addiction. At the time, the prevailing medical opinion was that the addiction process occurred in the stomach, and thus it was hypothesized that patients would not become addicted to morphine if it was injected into them via a hypodermic needle, and it was further hypothesized that this might potentially be able to cure opium addiction. However, many people did become addicted to morphine. In particular, addiction to opium became widespread among soldiers fighting in the Civil War, who very often required painkillers and thus were very often prescribed morphine. Women were also very frequently prescribed opiates, and opiates were advertised as being able to relieve "female troubles".[36]

Many soldiers in the Vietnam War were introduced to heroin and many developed a dependency to the substance which survived even when they returned to the US. Technological advances in travel meant that this increased demand for heroin in the US could now be met. Furthermore, as technology advanced, more drugs were synthesized and discovered, opening up new avenues to substance dependency.[36]

Society and culture

Legislation

Depending on the jurisdiction, addictive drugs may be legal, legal only as part of a government sponsored study, illegal to use for any purpose, illegal to sell, or even illegal to merely possess.

Most countries have legislation which brings various drugs and drug-like substances under the control of licensing systems. Typically this legislation covers any or all of the opiates, amphetamines, cannabinoids, cocaine, barbiturates, benzodiazepines, anesthetics, hallucinogenics, derivatives and a variety of more modern synthetic drugs. Unlicensed production, supply or possession is a criminal offence.

Usually, however, drug classification under such legislation is not related simply to addictiveness. The substances covered often have very different addictive properties. Some are highly prone to cause physical dependency, while others rarely cause any form of compulsive need whatsoever. Also, under legislation specifically about drugs, alcohol and nicotine are not usually included.

Although the legislation may be justifiable on moral or public health grounds, it can make addiction or dependency a much more serious issue for the individual: reliable supplies of a drug become difficult to secure, and the individual becomes vulnerable to both criminal abuse and legal punishment.

It is unclear whether laws against illegal drug use do anything to stem usage and dependency. In jurisdictions where addictive drugs are illegal, they are generally supplied by drug dealers, who are often involved with organized crime. Even though the cost of producing most illegal addictive substances is very low, their illegality combined with the addict's need permits the seller to command a premium price, often hundreds of times the production cost. As a result, addicts sometimes turn to crime to support their habit.

See also

- Addictive personality

- Drug and Alcohol Dependence (journal)
- Physical dependence
- Risk factors in pregnancy
- Self medication
- Stimulant maintenance
- Substance abuse
- Dual diagnosis

Questionnaires

- Alcohol Use Disorders Identification Test
- CAGE questionnaire
- CRAFFT Screening Test
- Paddington Alcohol Test
- Severity of Alcohol Dependence Questionnaire

References

1. 1 2 3 Malenka RC, Nestler EJ, Hyman SE (2009). "Chapter 15: Reinforcement and Addictive Disorders". In Sydor A, Brown RY. *Molecular Neuropharmacology: A Foundation for Clinical Neuroscience* (2nd ed.). New York: McGraw-Hill Medical. pp. 364–368. ISBN 9780071481274. "The defining feature of addiction is compulsive, out-of-control drug use, despite negative consequences. ...
   Addictive drugs are both rewarding and reinforcing. ... Familiar pharmacologic terms such as tolerance, dependence, and sensitization are useful in describing some of the time-dependent processes that underlie addiction. ...
   Dependence is defined as an adaptive state that develops in response to repeated drug administration, and is unmasked during *withdrawal*, which occurs when drug taking stops. Dependence from long-term drug use may have both a somatic component, manifested by physical symptoms, and an emotional–motivation component, manifested by dysphoria. While physical dependence and withdrawal occur with some drugs of abuse (opiates, ethanol), these phenomena are not useful in the diagnosis of addiction because they do not occur with other drugs of abuse (cocaine, amphetamine) and can occur with many drugs that are not abused (propranolol, clonidine).

   The official diagnosis of drug addiction by the Diagnostic and Statistic Manual of Mental Disorders (2000), which makes distinctions between drug use, abuse, and substance dependence, is flawed. First, diagnosis of drug use versus abuse can be arbitrary and reflect cultural norms, not medical phenomena. Second, the term substance dependence implies that dependence is the primary pharmacologic phenomenon underlying addiction, which is likely not true, as tolerance, sensitization, and learning and memory also play central roles. It is ironic and unfortunate that the Manual avoids use of the term addiction, which provides the best description of the clinical syndrome."
2. 1 2 "Substance use disorder". *Pubmed Health*. National Institutes of Health. Retrieved 12 September 2014. "Drug dependence means that a person needs a drug to function normally. Abruptly stopping the drug leads to withdrawal symptoms. Drug addiction is the compulsive use of a substance, despite its negative or dangerous effects"
3. ↑ Robison AJ, Nestler EJ (November 2011). "Transcriptional and epigenetic mechanisms of addiction". *Nat. Rev. Neurosci*. **12** (11): 623–637. doi:10.1038/nrn3111. PMC 3272277. PMID 21989194. "ΔFosB has been linked directly to several addiction-related behaviors ... Importantly, genetic or viral overexpression of ΔJunD, a dominant negative mutant of JunD which antagonizes ΔFosB- and other AP-1-mediated transcriptional activity, in the NAc or OFC blocks these key effects of drug exposure14,22–24. This indicates that ΔFosB is both necessary and sufficient for many of the changes wrought in the brain by chronic drug exposure. ΔFosB is also induced in D1-type NAc MSNs by chronic consumption of several natural rewards, including sucrose, high fat food, sex, wheel running,

where it promotes that consumption14,26–30. This implicates ΔFosB in the regulation of natural rewards under normal conditions and perhaps during pathological addictive-like states."

4. ↑ Blum K, Werner T, Carnes S, Carnes P, Bowirrat A, Giordano J, Oscar-Berman M, Gold M (2012). "Sex, drugs, and rock 'n' roll: hypothesizing common mesolimbic activation as a function of reward gene polymorphisms". *J. Psychoactive Drugs*. **44** (1): 38–55. doi:10.1080/02791072.2012.662112. PMC 4040958. PMID 22641964. "It has been found that deltaFosB gene in the NAc is critical for reinforcing effects of sexual reward. Pitchers and colleagues (2010) reported that sexual experience was shown to cause DeltaFosB accumulation in several limbic brain regions including the NAc, medial pre-frontal cortex, VTA, caudate, and putamen, but not the medial preoptic nucleus. Next, the induction of c-Fos, a downstream (repressed) target of DeltaFosB, was measured in sexually experienced and naive animals. The number of mating-induced c-Fos-IR cells was significantly decreased in sexually experienced animals compared to sexually naive controls. Finally, DeltaFosB levels and its activity in the NAc were manipulated using viral-mediated gene transfer to study its potential role in mediating sexual experience and experience-induced facilitation of sexual performance. Animals with DeltaFosB overexpression displayed enhanced facilitation of sexual performance with sexual experience relative to controls. In contrast, the expression of DeltaJunD, a dominant-negative binding partner of DeltaFosB, attenuated sexual experience-induced facilitation of sexual performance, and stunted long-term maintenance of facilitation compared to DeltaFosB overexpressing group. Together, these findings support a critical role for DeltaFosB expression in the NAc in the reinforcing effects of sexual behavior and sexual experience-induced facilitation of sexual performance. ... both drug addiction and sexual addiction represent pathological forms of neuroplasticity along with the emergence of aberrant behaviors involving a cascade of neurochemical changes mainly in the brain's rewarding circuitry."
5. ↑ Olsen CM (December 2011). "Natural rewards, neuroplasticity, and non-drug addictions". *Neuropharmacology*. **61** (7): 1109–22. doi:10.1016/j.neuropharm.2011.03.010. PMC 3139704. PMID 21459101.
6. ↑ "Diagnostic criteria for Substance Dependence: DSM IV–TR". *BehaveNet*. Retrieved 12 June 2015.
7. ↑ "Substance Dependence". *BehaveNet*. Retrieved 12 June 2015.
8. 1 2 Malenka RC, Nestler EJ, Hyman SE (2009). "Chapter 15: Reinforcement and Addictive Disorders". In Sydor A, Brown RY. *Molecular Neuropharmacology: A Foundation for Clinical Neuroscience* (2nd ed.). New York: McGraw-Hill Medical. pp. 364–375. ISBN 9780071481274.
9. ↑ Nestler EJ (December 2013). "Cellular basis of memory for addiction". *Dialogues Clin. Neurosci*. **15** (4): 431–443. PMC 3898681. PMID 24459410.
10. ↑ "Glossary of Terms". *Mount Sinai School of Medicine*. Department of Neuroscience. Retrieved 9 February 2015.
11. ↑ Volkow ND, Koob GF, McLellan AT (January 2016). "Neurobiologic Advances from the Brain Disease Model of Addiction". *N. Engl. J. Med*. **374** (4): 363–371. doi:10.1056/NEJMra1511480. PMID 26816013.
12. ↑ Nutt King, Saulsbury , Blakemore (2007). "Development of a rational scale to assess the harm of drugs of potential misuse". *Lancet*. **369** (9566): 1047–53. doi:10.1016/S0140-6736(07)60464-4. PMID 17382831.
13. ↑ "Marijuana Drug Facts". National Institute on Drug Abuse. January 2014. Retrieved 18 April 2014.
14. ↑ "Dangerousness of Drugs A Guide To The Risks And Harms Associated With Substance Misuse" (PDF). National Addiction Center. Retrieved 6 May 2014.
15. ↑ AJ Giannini, RQ Quinones, DM Martin. Role of beta-endorphin and cAMP in addiction and mania. Society for Neuroscience Abstracts. 15:149, 1998.
16. ↑ Boob G, Kreek MJ (2007). "Stress, Dysregulation of Drug Reward Pathways, and the Transition to Drug Dependence". *Am J Psychiatry*. **164** (8): 1149–59. doi:10.1176/appi.ajp.2007.05030503. PMC 2837343. PMID 17671276.
17. ↑ Ball JC, van de Wijngaart GF (1994). "A Dutch addict's view of methadone maintenance—an American and a Dutch appraisal". *Addiction*. **89** (7): 799–802; discussion 803–14. doi:10.1111/j.1360-0443.1994.tb00974.x. PMID 8081178.
18. ↑ Reynolds M, Mezey G, Chapman M, Wheeler M, Drummond C, Baldacchino A (2005). "Co-morbid post-traumatic stress disorder in a substance misusing clinical population". *Drug Alcohol Depend*. **77** (3): 251–8. doi:10.1016/j.drugalcdep.2004.08.017. PMID 15734225.
19. ↑ Moggi F, Giovanoli A, Strik W, Moos BS, Moos RH (2007). "Substance use disorder treatment programs in Switzerland and the USA: Program characteristics and 1-year outcomes". *Drug Alcohol Depend*. **86** (1): 75–83. doi:10.1016/j.drugalcdep.2006.05.017. PMID 16782286.

20. ↑ Nils Bejerot: Swedish addiction epidemic in an international perspective, 1988
21. ↑ Giannini AJ (June 1996). "Alexithymia, affective disorders and substance abuse: possible cross-relationships". *Psychol Rep*. **78** (3 Pt 2): 1389–90. doi:10.2466/pr0.1996.78.3c.1389. PMID 8816054.
22. ↑ DAA/UK
23. ↑ Schaler, Jeffrey Alfred (1997). "Addiction Beliefs of Treatment Providers: Factors Explaining Variance". *Addiction Research & Theory*. **4** (4): 367–384. doi:10.3109/16066359709002970. ISSN 1476-7392.
24. ↑ O'Donohue, W; K.E. Ferguson (2006). "Evidence-Based Practice in Psychology and Behavior Analysis" (PDF). *The Behavior Analyst Today*. Joseph D. Cautilli. **7** (3): 335–350.
25. ↑ Chambless, D.L. (1998). "An update on empirically validated therapies" (PDF). *Clinical Psychology*. American Psychological Association. **49**: 5–14.
26. ↑ Dutcher LW, Anderson R, Moore M, Luna-Anderson C, Meyers RJ, Delaney HD, Smith JE (Spring 2009). "Community Reinforcement and Family Training (CRAFT): An Effectiveness Study" (PDF). *Journal of Behavior Analysis of Sports, Health Fitness and Behavioral Medicine*. **2** (1): 82–93. ISSN 1946-7079.
27. ↑ Meyers RJ, Smith JE, Lash DN (June 2005). "A Program for Engaging Treatment-Refusing Substance Abusers into Treatment: CRAFT" (PDF). *IJBCT*. **1** (2): 90–100. ISSN 1555-7855.
28. ↑ Smith JE, Milford JL, Meyers RJ (2004). "CRA and CRAFT: Behavioral Approaches to Treating Substance-Abusing Individuals" (PDF). *The Behavior Analyst Today*. **5** (4): 391–403.
29. ↑ http://www.ama-assn.org/ama1/pub/upload/mm/21/omss-handbook-final.pdf
30. ↑ Jordan JB (2006). "Acupuncture treatment for opiate addiction: a systematic review". *J Subst Abuse Treat*. **30** (4): 309–14. doi:10.1016/j.jsat.2006.02.005. PMID 16716845.
31. ↑ White AR, Rampes H, Campbell JL (2006). White, Adrian R, ed. "Acupuncture and related interventions for smoking cessation". *Cochrane Database Syst Rev* (1): CD000009. doi:10.1002/14651858.CD000009.pub2. PMID 16437420.
32. ↑ "Treatment Approaches for Drug Addiction", *National Institute of Drug Abuse*, 09/12/12
33. ↑ Lowinson, Joyce H; Ruiz, Pedro; Millman, Robert B; Langrod, John G (eds) (2005). *Substance Abuse: A Comprehensive Textbook* (4th ed.). Philadelphia: Lippincott Williams & Wilkins. ISBN 0-7817-3474-6
34. ↑ Hillman, D.C.A. (22 July 2008). *The chemical muse: drug use and the roots of Western civilization*. Macmillan. ISBN 978-0-312-35249-3.
35. ↑ Rinella, Michael A. (23 November 2011). *Pharmakon: Plato, Drug Culture, and Identity in Ancient Athens*. Rowman & Littlefield. ISBN 978-0-7391-4687-3.
36. 1 2 3 Casey, Elaine. "History of Drug Use and Drug Users in the United States". *www.druglibrary.org*. Retrieved 3 January 2014.

Comer, Ronald J, (2013). Substance-Related Disorders. In Abnormal Psychology (Eighth ed., Vol. 1, pp. 1–589). New York, NY: Worth.

External links

- American Society of Addiction Medicine website
- Health-EU Portal – Drugs
- people, drug addicts
- Trips Beyond Addiction | Living Hero Radio Show and Podcast special. With Dimitri Mobengo Mugianis, Bovenga Na Muduma, Clare S. Wilkins, Brad Burge, Tom Kingsley Brown, Susan Thesenga, Bruce K. Alexander, PhD ~ the voices of ex-addicts, researchers from The Multidisciplinary Association for Psychedelic Studies and Ibogaine/Iboga/Ayahuasca treatment providers sharing their experiences in breaking addiction with native medicines. January 2013
- A social history of America's most popular drugs.
- National Institute on Drug Abuse: "NIDA for Teens: Brain and Addiction".
- "WHO Expert Committee on Drug Dependence – WHO Technical Report Series, No. 915 – Thirty-third

Report". *apps.who.int*. 2003. Retrieved 26 February 2015. - pdf

Psychoactive substance-related disorder (F10–F19, 291–292; 303–305)

General	SID (Substance intoxication / Drug overdose · Withdrawal · Substance-induced psychosis) · SUD (Substance abuse · Physical dependence / Substance dependence)			
Alcohol	**SID**	**Diseases**	**Neurological disorders**	Alcoholic hallucinosis · Alcohol withdrawal · Fetal alcohol spectrum disorder (FASD) · Fetal alcohol syndrome (FAS) · Korsakoff's syndrome · Wernicke–Korsakoff syndrome · Wernicke's encephalopathy
			Digestive system	Alcoholic hepatitis · Alcoholic liver disease · Auto-brewery syndrome
			Nervous system	Alcohol-related dementia · Alcoholic hallucinosis · Hangover
			Cardiovascular system	Alcoholic cardiomyopathy · Alcohol flush reaction
	SUD	Alcoholism · Alcohol dependence · Alcohol abuse		
Opioids	SID (Opioid overdose) · SUD (Opioid addiction and dependence)			
Caffeine	SID (Effect of caffeine on memory · Caffeine-induced sleep disorder) · SUD (Caffeine dependence)			
Cannabis	SID (Effects of cannabis · Long-term effects of cannabis) · SUD (Cannabis dependence)			
Sedative / hypnotic	*benzodiazepine:* SID (Benzodiazepine overdose · Benzodiazepine withdrawal) · SUD (Benzodiazepine misuse · Benzodiazepine dependence) · *barbiturate:* SID (Barbiturate overdose) · SUD (Barbiturate dependence)			
Cocaine	SID (Cocaine intoxication) · SUD (Cocaine dependence)			
Stimulants	SID (Stimulant psychosis) · SUD (Amphetamine dependence)			
Hallucinogen	SID (Hallucinogen persisting perception disorder)			
Tobacco	SID (Nicotine poisoning · Nicotine withdrawal)			
Volatile solvent	Inhalant abuse: Toluene toxicity			
Multiple	Poly drug use			

Reinforcement disorders: Addiction and Dependence		
Addiction	**Drug**	Alcoholism · Amphetamine · Cocaine · Ethanol · Methamphetamine · Methylphenidate · Nicotine · Opioid
	Behavioral	Financial (Gambling · Shopping) · Media (Computer · Internet · Video game) · Palatable food · Sex-related (Cybersex · Intercourse · Pornography)
	Cellular mechanisms	Transcriptional (**ΔFosB** · c-Fos · Cdk5 · CREB · GluR2 · NF-κB) Epigenetic (**G9a** · G9a-like protein · **HDAC1** · **HDAC2** · **HDAC3** · HDAC4 · HDAC5 · HDAC9 · HDAC10 · SIRT1 · SIRT2 · ...)
Dependence	**Concepts**	Physical dependence · Psychological dependence · Withdrawal
	Disorders	Alcoholism · Amphetamine · Barbiturate · Benzodiazepine · Caffeine · Cannabis · Cocaine · Nicotine · Opioid · Substituted amphetamine
See also	Category:Addiction · Cognitive behavioral therapy · Harm reduction · Support groups (Addiction recovery groups · List of twelve-step groups · NoFap)	