

Continue



By the end of this section, you will be able to:Describe the relationship between drug tolerance and withdrawalIdentify the neurotransmitter systems impacted by various categories of drugsDescribe how different categories of drugs affect behaviour and experienceWhile we all experience altered states of consciousness in the form of sleep on a regular basis, it is people who use substances that are used to alter states of consciousness who are most interested in the effects of substances on their minds. The effects of substances on the mind are commonly used today. Drugs exert their effects on both physical and psychological bodily functions. Physical dependenceinvolves changes in normal bodily functionsover the use of a substance. In contrast, a person who haspsychological dependencehas an emotional, rather than physical, need for the drug and may use the drug to relieve psychological distress.Toleranceis linked to physiological dependence, and it occurs when a person requires more and more drug to achieve effects previously experienced at lower doses. Tolerance can cause the user to increase the amount of drug used to a dangerous leveleven to the point of overdose and death.Drugwithdrawalincludes a variety of negative symptoms experienced when drug use is discontinued. These symptoms usually are opposite of the effects of the drug. For example, withdrawal from sedative drugs often produces unpleasant arousal and agitation. In addition to withdrawal, many individuals who are diagnosed with substance use disorders will also develop tolerance to these substances. Psychological dependence, or drug craving, is a recent addition to the diagnostic criteria for substance use disorder in DSM-5. This is an important factor because we can develop tolerance and experience withdrawal from any number of drugs that we do not abuse. In other words, physical dependence in and of itself is of limited utility in determining whether or not someone has a substance use disorder. The effects of all psychoactive drugs occur through their interactions with our endogenous neurotransmitter systems. Many of these drugs, and their relationships, are shown inTable SC.2. As you have learned, drugs can act as agonists or antagonists of a given neurotransmitter system. An agonist facilitates the activity of a neurotransmitter system, and antagonists impede neurotransmitter activity.Table SC.2 Drugs and Their EffectsClass of DrugExamplesEffects on the BodyEffects When UsedPsychologically Addicting?StimulantsCocaine, amphetamines (including some ADHD medications), such as Adderall, methamphetamines, MDMA (Ecstasy or Molly),increases heart rate, blood pressure, body temperature,causes euphoria, decreases alertness,paranoia can cause hallucinations,Some are addictive, some are not.Sensitization to physical stimuli: High doses of MDMA can cause brain toxicity and death.YesSedative/Hypnotic/DepressantsAlcohol, barbiturates (e.g., secobarbital, pentobarbital), Benzodiazepines (e.g., Xanax)Decreases heart rate, blood pressureLow dose increase relaxation, decrease inhibitions. High doses can induce sleep, cause motor disturbance, memory loss, decreased respiratory function, and death.YesOpiatesOpiium, Heroin, Fentanyl, Morphine, Oxycodone, Vicodin, methadone, and other prescription pain relieversDecreased pain, pupil dilation, decreased gut motility, decreased respiratory functionPain relief, euphoria, sleepiness. High doses can cause death due to respiratory depression.YesHallucinogensMarijuana, LSD, Peyote, mescaline, DMT, dissociative anesthetics including ketamine and PCPincrease heart rate and blood pressure that may dissipate over timeMild to intense perceptual changes with high variability in effects based on strain, method of ingestion, and individual differencesYesThe Genetic Science Learning Centre at the University of Utah, created an interactive (simplified) overview of the mechanism and effects of several common drugs. You can access and interact with Mouse Party here: that this activity requires the Flash Player plug-in. For individuals who cannot view this activity, we have created a walkthrough video to show each of the mice and the drug effects and mechanisms. If the video above does not load, click here: a drug that tends to suppress central nervous system activity(Figure SC.15). Some depressants include alcohol, barbiturates and benzodiazepines. These drugs share in common their ability to serve as agonists of the gamma-Aminobutyric acid (GABA) neurotransmitter system. Because GABA has a quieting effect on the brain, GABA agonists also have a quieting effect; these types of drugs are often prescribed to treat both anxiety and insomnia.Figure SC.15The GABA-gated chloride (Cl) channel is embedded in the cell membrane of certain neurons. The channel has multiple receptor sites where alcohol, barbiturates, and benzodiazepines bind to exert their effects. The binding of these molecules opens the chloride channel, allowing negatively-charged chloride ions (Cl-) into the neurons cell body. Changing its charge in a negative direction pushes the neurons away from firing; thus, activating GABA neurons causes a net inhibiting effect of the brain.Ethanol, which we commonly refer to as alcohol, is in a class of psychoactive drugs known as depressants. Acute alcohol administration results in a variety of changes to consciousness. At rather low doses, alcohol use is associated with feelings of euphoria. As the dose increases, people report feeling sedated. Generally, alcohol is associated with decreases in reaction time and visual acuity, lowered levels of alertness, and reduction in behavioural control. With excessive alcohol use, a person might experience a complete loss of consciousness and/or difficulty remembering events that occurred during a period of intoxication (McKim & Hancock, 2013). In addition, if a pregnant woman consumes alcohol, her infant may be born with a cluster of birth defects and symptoms collectively called fetal alcohol spectrum disorder (FASD) or fetal alcohol syndrome (FAS). With repeated use of many central nervous system depressants, such as alcohol, a person becomes physically dependent upon the substance and will exhibit signs of both tolerance and withdrawal. Psychological dependence on these drugs is also possible. Therefore, the abuse potential of central nervous system depressants is relatively high. Drug withdrawal is usually an aversive experience, and it can be a life-threatening process in individuals who have a long history of very high doses of alcohol and/or barbiturates. This is of such concern that people who are trying to overcome addiction to these substances should only do so under medical supervision. Stimulantsare drugs that tend to increase overall levels of neural activity. Many of these can act as agonists of the dopamine neurotransmitter system. Dopamine activity is often associated with reward and craving; therefore, drugs that affect dopamine neurotransmission often have abuse liability. Drugs in this category include cocaine, amphetamines (including methamphetamine), and cathinones (i.e., bath salts), MDMA (ecstasy), nicotine, and caffeine. Cocaine can be taken in multiple ways. While many users snort cocaine, intravenous injection and inhalation (smoking) are also common. The freebase version of cocaine, known as crack cocaine, is particularly addictive. Like many other stimulants, cocaine blocks the dopamine reuptake system by blocking the dopamine transporter system. Methamphetamine is another stimulant drug. Methamphetamine is a synthetic amphetamine derivative. Methamphetamine is a powerful stimulant that reaches the brain very quickly to produce an intense euphoria that dissipates almost as fast as it arrives, prompting users to continuing taking the drug. Users often consume the drug every few hours across days-long binges called runs, in which the user forgoes food and sleep. In the wake of the opiate epidemic, many drug cartels in Mexico are shifting from producing heroin to producing highly potent but inexpensive forms of methamphetamine. The low cost coupled with lower risk of overdose than with opiate drugs is making crystal meth a popular choice among drug users today (NIDA, 2019). Using crystal meth poses a number of serious long-term health issues, including dental problems (often called meth mouth), skin abrasions caused by excessive scratching, memory loss, sleep problems, violent behaviour, paranoia, and hallucinations. Methamphetamine addiction produces an intense craving that is difficult to treat.Amphetamines have a mechanism of action quite similar to cocaine in that they block the reuptake of dopamine in addition to stimulating its release (Figure SC.16). While amphetamines are often abused, they are also commonly prescribed to children diagnosed with attention deficit hyperactivity disorder (ADHD). It may seem counterintuitive that stimulant medications are prescribed to treat a disorder that involves hyperactivity, but the therapeutic effect comes from increases in neurotransmitter activity within certain areas of the brain associated with impulse control. These brain areas include the prefrontal cortex and basal ganglia.Figure SC.16As one of their mechanisms of action, cocaine and amphetamines block the reuptake of dopamine from the synapse into the presynaptic cell.In recent years, methamphetamine (meth) use has become increasingly widespread.Methamphetamineis a type of amphetamine that can be made from ingredients that are readily available (e.g., medications containing pseudoephedrine, a compound found in many over-the-counter cold and flu remedies). Despite recent changes in laws designed to make it more difficult to produce, methamphetamine continues to be an easily accessible and relatively inexpensive drug option. Shukly, Crum, and Christy (2013) conducted a case study of a 40-year-old woman who suffered significant ill effects from her use of caffeine. The woman used caffeine in the past to boost her mood and to provide energy, but over the course of several years, she increased her psychoactive drugs known as depressants. 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While many users snort cocaine, intravenous injection and inhalation (smoking) are also common. The freebase version of cocaine, known as crack cocaine, is particularly addictive. Like many other stimulants, cocaine blocks the dopamine reuptake system by blocking the dopamine transporter system. Methamphetamine is another stimulant drug. While it is probably the most commonly used drug in the world, the potency of this particular drug pales in comparison to the other stimulant drugs described in this section. Generally, people use caffeine to maintain increased levels of alertness and arousal. Caffeine is found in many common medicines (such as weight loss drugs), beverages, foods, and even cosmetics (Herman & Herman, 2013). While caffeine may have some indirect effects on dopamine neurotransmission, its primary mechanism of action involves antagonizing adenosine activity (Porkka-Heiskanen, 2011). Adenosine is a neurotransmitter that promotes sleep. Caffeine is an adenosine antagonist, so caffeine inhibits the adenosine receptors, thus decreasing sleepiness and promoting wakefulness.While caffeineis generally considered a relatively safe drug, high blood levels of caffeine can result in insomnia, agitation, muscle twitching, nausea, irregular heartbeat, and even death (Kensler, Strain, & Griffith, 2009; Wolf, Ganetsky, & Babu, 2012). In 2012, Kravtsov and Nielson reported on a case study of a 40-year-old woman who suffered significant ill effects from her use of caffeine. The woman used caffeine in the past to boost her mood and to provide energy, but over the course of several years, she increased her caffeine consumption to the point that she was consuming three litres of soda each day. Although she had been taking a prescription antidepressant, her symptoms of depression continued to worsen and she began to suffer physically, displaying significant warning signs of cardiovascular disease and diabetes. Upon admission to an outpatient clinic for treatment of mood disorders, she met all of the diagnostic criteria for substance dependence and was advised to dramatically limit her caffeine intake. Once she was able to limit her use to less than 12 ounces of soda a day, both her mental and physical health gradually improved. Despite the prevalence of caffeine use and the large number of people who confess to suffering from caffeine addiction, this was the first published description of soda dependence appearing in scientific literature.Nicotine is highly addictive, and the use of tobacco products is associated with increased risks of heart disease, stroke, and a variety of cancers. Nicotine exerts its effects through its interaction with acetylcholine receptors. Acetylcholine functions as a neurotransmitter in motor neurons. In the central nervous system, it plays a role in arousal and reward mechanisms. Nicotine is most commonly used in the form of tobacco products like cigarettes or chewing tobacco; therefore, there is a tremendous interest in developing effective smoking cessation techniques. To date, people have used a variety ofnicotinerplacement therapies in addition to various psychotherapeutic options in an attempt to discontinue their use of tobacco products. In general, smoking cessation programs may be effective in the short term, but it is unclear whether these effects persist (Cropley, Theadom, Pravettoni, & Webb, 2008; Lavit, Shaw, Wong, & Kaczorowski, 2017; Smedslund, Fiser, Bostin, & Lichtenstein, 2014). Vaping as a means to deliver nicotine is becoming increasingly popular, especially among teens and young adults. Vaping uses battery-powered devices, sometimes called e-cigarettes, that deliver liquid nicotine and flavors in a vapour. Originally reported as a safe alternative to the known cancer-causing agents found in cigarettes, vaping is now known to be very dangerous and has led to serious lung disease and death in users. Anopiodis a category of drugs that includes heroin, methadone, and codeine. Opioids have analgesic properties; that is, they decrease pain. Humans have an endogenous opioid neurotransmitter systemthe body makes small quantities of opioid compounds that bind to opioid receptors reducing pain and producing euphoria. Thus, opioid drugs, which mimic this endogenous painkilling mechanism, have an extremely high potential for abuse. Natural opioids, calledopiates, are derivatives of opium, which is a naturally occurring compound found in the poppy plant. There are now several synthetic versions of opiate drugs (correctly called opioids) that have very potent painkilling effects, and they are often abused. For example, the National Institutes of Drug Abuse has sponsored research that suggests the misuse and abuse of the prescription pain killers hydrocodone and oxycodone are significant public health concerns (Maxwell, 2006). In 2013, the U.S. Food and Drug Administration recommended tighter controls on their medical use.Historically, heroin has been a major opioid drug of abuse (Figure SC.17). Heroin can be snorted, smoked, or injected intravenously. Heroin produces intense feelings of euphoria and pleasure, which are amplified when the heroin is injected intravenously. Following the initial rush, users experience 46 hours of going on the nod, alternating between conscious and semiconscious states. Heroin users often shoot the drug directly into their veins. Some people who have injected many times into their arms will show track marks, while other users will inject into areas between their fingers or between their toes, so as not to show obvious track marks and, like all abusers of intravenous drugs, have an increased risk for contraction of both tuberculosis and HIV.Figure SC.17(a) Common paraphernalia for heroin preparation and use are shown here in a needle exchange kit. (b) Heroin is not supposed to be injected. A notable case of work by Todd Hufnagel, aside from their primary use as anesthetic drugs, opiate-like compounds are also found in rough suppressants, anti-nausea, and anti-diarrheal medications. The withdrawal from a drug often involves an experience opposite to the effect of the drug. It should be noted that opiod withdrawal resembles a severe case of the flu. While opiod withdrawal can be extremely unpleasant, it is not life-threatening (Jude, 2005). 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It seems like everyone knows a friend, family member, or neighbour who has died of an overdose. Opioid addiction reached crisis levels in the United States such that by 2019, an average of 130 people diedeach dayof an opiod overdose (NIDA, 2019). The crisis actually began in the 1990s, when pharmaceutical companies began mass-marketing pain-relieving opiod drugs like Oxycotin with the promise (now known to be false) that they were non-addictive. Increased prescriptions led to greater rates of misuse, along with greater incidence of addiction, even among patients who used these drugs as prescribed. Physiologically, the body can become addicted to opiate drugs in less than a week, including when taken as prescribed. Withdrawal from opioids includes pain, which patients often misinterpret as pain caused by the problem that led to the original prescription, and which motivates patients to continue using the drugs. 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Use is required to clarify such effects, it is certainly possible to measure peoples beliefs about the nature of and explanations of consciousness as well as psychedelic experiences tend to impact such beliefs. The scientific study of psychedelics and consciousness, in all of its meanings, is still nascent. While we cannot, at present, see any clear scientific track resulting from the intersection of psychedelics and the hard problem of consciousness, we are open to the possibility of being proven wrong. We find the relationship between psychedelics and consciousness (in every sense) fascinating, but we also believe that it is important to be clear about which sense of the term consciousness is being used at any given time and to ensure claims regarding explanations of phenomenal consciousness are differentiated from claims about the contents of consciousness (which includes the set of changes to perception, affect, and cognition in what are called altered states of consciousness). We believe this is essential for clear communication among scientists as well as in public science communication (Johnson, 2020). While psychedelics surely impact many phenomena associated with the easy problems of consciousness (though they may not do so uniquely), we believe epistemic humility is called for regarding the potential for psychedelics to illuminate the hard problem of consciousness. Due to the epistemological questions surrounding consciousness, it currently appears unlikely that psychedelics, like other extant scientific tools, could be used to definitively explain the existence of or biological basis of phenomenal consciousness (i.e., solve the hard problem); however, psychedelics are proving useful tools for researchers investigating many of the so-called easy problems of consciousness, and it seems likely that their full potential to facilitate scientific advances is only beginning to be tapped.We thank Dr Chris Letheby for helpful comments on the manuscript. This work was supported by Tim Ferriss, Matt Mulenweg, Blake Mycoskie, Craig Nerenberg, and the Steven and Alexandra Cohen Foundation for Drs D. Yaden, M. Johnson, R. Griffiths, A. Garcia-Romeu, S. Nayak, N. Gukasyan, and F. Barrett through the Johns Hopkins Center for Psychedelic and Consciousness Research. This work was supported by the National Institute on Alcohol Abuse and Alcoholism of the National Institutes of Health (grant no. R01AA024845) for Dr B. Mathur. This work was supported by the National Institute on Drug Abuse (grant no. T32DA07209) for Drs Gukasyan and Doss.Dr Barrett is a scientific advisor for WavePaths, LLC, which develops music-based interventions for psychedelic therapies. Dr R. Griffiths is on the board of directors of the Heffter Research Institute. Dr Griffiths has also received grants for research from the Riverstyx Foundation and a crowd-sourced funding campaign organized by Tim Ferriss. Dr M. Johnson is in paid advisory relationships with the following organizations regarding the medical development of psychedelics or related compounds: AWAKN Life Sciences Inc., Beckley Psychedelic Ltd., Entheogen Biomedical Corp., Field Trip Psychedelics, Inc., Mind Medicine, Inc., Otsuka Pharmaceutical Development and Commercialization, Inc., and Silo Pharma, Inc. The other authors have no disclosures to report. Drs A. Garcia-Romeu and S. Nayak serve on a Data and Safety Monitoring Board for Maryland Oncology Hematology. Dr Garcia-Romeu is a scientific advisor for ETHA Natural Botanicals and NeonMind Bioscience.Atlan G, Terem A, Peretz-Rivlin N, Schrawat K, Gonzales BJ, Pozner G, Tasaka GI, Goll Y, Refaeli R, Zviran O, Lim BK, Groysman M, Goshen I, Mizrahi A, Nelken I, Citri A (2018) The claustrum supports resilience to distraction. *Curr Biol*28:2752-2762.e7. [DOI] [PMC free article] [PubMed] [Google Scholar]Baars BJ (1993) A cognitive theory of consciousness. 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