

Never Enough: The Neuroscience and Experience of Addiction	
Author	Judith Grisel - BA in Psychology (Florida Atlantic University), MA in Behavioral Neuroscience/Psychology (University of Colorado), PhD in Behavioral Neuroscience/Psychology (University of Colorado)
Statistics	About 16% of the population 12 and older meet criteria for a substance use disorder 10,000 people around the globe die each day as a result of substance abuse No more than 10% of substance abusers can manage to stay clean for any appreciable time
Causes of addiction	Addiction results from a web of factors, including a genetic predisposition, developmental influences, and environmental input We are unable to predict whether a particular individual will develop an addiction Enough exposure to any mind-altering drug will induce tolerance and dependence - Eventually, exposure to a favorite drug results in virtually no change in dopamine, but withholding it leads to a big drop
Hedonism leads to discontentment	Despite arranging things to my own liking, by eliminating limits and responsibilities and partying nonstop—I was entirely discontented
Irony of drug use	I'd sought wellness and became sick; fun, but lived in a constant state of anxious dread; freedom, and was enslaved
Sensory limitations	Many insects can see ultraviolet light that for us is invisible We can't hear very high- or low-pitched sounds
Dopamine	All addictive drugs are addictive precisely because they share the ability to stimulate the mesolimbic dopamine system The mesolimbic system evolved to promote behaviors such as eating and sex Dopamine in the mesolimbic pathway works not by signaling pleasure but by signaling the anticipation of pleasure Dopamine in the nigrostriatal pathway enables us to take action either toward or away from a stimulus
3 Laws of Psychopharmacology	All drugs act by changing the rate of what is already going on - Drugs can either speed up or slow down ongoing neural

	activity—and that's it - Drugs work by mimicking neurotransmitters and binding to the receptor sites designed to interact with them All drugs have side effects - Unlike normal neurotransmitters, drugs are not targeted in their delivery to precise cells or circuits and are found throughout the nervous system, acting at all accessible targets The brain adapts to all drugs that affect it by counteracting the drug's effects - The brain's response to a drug is always to facilitate the opposite state
Tolerance	The first cigarette of the day is the best one because after the particular brain sites for nicotine's effects have been activated, they become insensitive to subsequent exposures A user must take more and more to produce the same high Repeated encounters with the stimulus result in faster, bigger, and longer-lasting processes that are better able to maintain homeostasis in the face of disruption - Withdrawal happens because this process outlasts the drug's effects - Craving occurs because any environmental signal that has been associated with the drug can itself elicit this process that can only be assuaged by indulging in the drug - By drinking regularly at certain times, he feels the longing for liquor at the stated return of these periods
Getting rid of craving	Following detox (after several weeks of clean time), the addict is exposed to cues that used to coincide with using, but within a supportive, therapeutic context - With repeated exposure and no drug delivery, craving dissipates
Marijuana	It can make some people sleepy, and others paranoid due to a confluence of neurobiology and genetics It accentuates attributes of environmental stimuli: music is amazing, food delicious, jokes hilarious, colors rich THC (or delta-9-tetrahydrocannabinol) is the active ingredient in marijuana The downside is that on rare occasions, when I was not high, I could barely feign interest in anything

	- The world on the drug seemed so much shinier than the world without it
Opiates	Narcotics is the umbrella term for all opiate drugs More people die of narcotic overdoses than automobile accidents About 4 out of 5 heroin users start by misusing prescription painkillers and turn to street narcotics because they are cheaper and easier to get Narcotics work by mimicking endorphins, the body's natural painkillers Because an addict's nervous system is regularly flooded with compounds that produce euphoria, the anti-opiate system ramps up to create pain The degree of tolerance, dependence, and craving in opiate users is stronger than for almost every other drug
Treatment	Giving anti-opiates should induce the brain to maintain homeostasis by upregulating, or at least normalizing, its opioid system
Types of drugs	Stimulants increase activity Hallucinogens alter perception Sedative-hypnotics slow brain activity and promote sleep Opiates/narcotics relieve pain
Alcohol	Alcohol is classified as a sedative-hypnotic I am particularly curious about the general practice of celebrating peak experiences with a sedative It seems odd that we drink and use to permit or enhance strong feelings, as well as to mute them As Socrates noted, sorrow and joy depend on each other - It is likely impossible to tamp down terror without also leveling pleasure Because alcohol reduces anxiety, this drug will be more reinforcing to those who are naturally anxious If someone finds alcohol especially rewarding because of an inherited tendency toward anxiety and imbibes frequently, they'll become increasingly anxious

	Alcohol slows neural activity throughout the brain - Explains the drug's global effects on cognition, emotion, memory, and movement Those who have a positive family history of alcoholism are 3 to 5 times more likely to develop the disease Even one drink a day is associated with a number of diseases, including cancers and cardiovascular issues It takes less alcohol for women to achieve the same blood concentrations as men
Punishment vs reinforcement	Punishment is not an especially effective way to change behavior Somehow, the threat of losing everything is usually insufficient for addicts inclined to pick up
Caffeine	Most popular psychoactive drug in the world Regular use will likely cause dependence (that is, withdrawal upon abstinence) Benefits of regular caffeine use include improvements in mood, memory, alertness, and physical and cognitive performance - It improves athletic performance and endurance About half the people who drink it regularly will experience headaches if they suddenly withdraw
Nicotine	More than 7 million die each year from their addiction On average, tobacco users lose 15 years of life E-cigarettes and marijuana are likely to be less harmful to physical health, primarily because the vehicle for nicotine in smoked tobacco is well known to be carcinogenic Most regular smokers consume 2 to 3 cigarettes an hour Withdrawal produces craving characterized by irritability, anxiety, attention deficits, trouble sleeping, and increased appetite
Methamphetamine	Has at least 37 million users—about twice the number of either cocaine or heroin Effects from low to moderate doses include euphoria, wakefulness, increased confidence, hyperactivity, and loss of appetite

	Addiction devolves into tolerance to meth's euphoric effects and sensitization to cognitive stress systems
Drug schedules	Schedule I drugs are considered to have the highest potential for abuse and dependence, and Schedule V the least
Psychedelics	Majority of scientists don't think these are addictive - Tolerance is so fast that it precludes regular use LSD gave me an inner joy, an open-mindedness, a gratefulness, open eyes, and an internal sensitivity for the miracles of creation The use of LSD in the drug scene can be seen as a profanation of a sacred substance - If it had been subjected to the same taboos and the same reverence the Indians had, LSD would never have had such a bad reputation They don't cause dopamine release in the nucleus accumbens DMT reportedly produces vivid mystical experiences, euphoria, and hallucinations especially of geometric forms, higher intelligences, extraterrestrials, elves, and God Acid trips helped me realize at a critical time in my psychosocial development that I was not the center of anything Researchers found a 25% decreased likelihood of theft or other property crime, and an 18% decreased likelihood of violent crime, in those who used psychedelics - Use of other drugs including cocaine, heroin, marijuana, and MDMA were all associated with increased risk for committing these crimes
What leads to addiction?	An inherited biological disposition, copious drug exposure, particularly during adolescence, and a catalyzing environment
Changing names	We've used "addict" or "alcoholic" and then "drug dependent"; now we talk about having a drug use disorder - Changing names or diagnostic criteria in the DSM might provide an illusion of progress, but I think it just makes it clear how little we truly understand
Intellectual humility	The more closely we examine any aspect of reality, the more we see how much there is to learn - Complexity, ambiguity, and contingencies are the rule in all of nature The majority of scientific progress is measured by improvements in the questions we ask rather than the finality of our answers

Solutions	After many decades in the field, I'm increasingly skeptical that the solutions are ever going to be found solely in the brain One of the most effective ways to curtail the risk of addiction is to avoid intoxication during periods of rapid brain development Federal agents, friends' deaths, expulsions and evictions, physical withdrawal, and myriad other tragedies weren't enough to propel me to change; instead, it was human love and connection Disordered use comes from, thrives in, and creates alienation
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