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Drug Addiction and Its Effects on the Brain

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ABSTRACT: Drug addiction is a chronic, relapsing brain disorder in which people keep seeking and using drugs despite harmful consequences. This review covers why people start using drugs, the biological, environmental and developmental factors that raise the risk of addiction, and the brain changes behind the move from voluntary use to compulsive use. Genetic and epigenetic factors are estimated to account for 40–60% of a person's vulnerability. Starting drug use early, during adolescence, and taking drugs by smoking or injection make addiction more likely, which shows why prevention matters while the brain is still developing.

Three brain regions are central to the disorder. The basal ganglia hold the reward circuit, the extended amygdala drives stress and negative emotion, and the prefrontal cortex controls executive function and self-control. Addiction is described as a three-stage cycle:

Binge/intoxication: dopamine release in the nucleus accumbens drives reward and conditioned learning to drug cues.

Withdrawal/negative affect: dopamine responses become blunted, natural rewards feel less rewarding, and the brain's stress systems (CRF, dynorphin) are recruited.

Preoccupation/anticipation: dopamine and glutamate signalling in the prefrontal cortex is disrupted, which weakens self-control and supports craving and relapse.

The review also looks at how tonic and phasic dopamine firing work, and at the different roles of D1 and D2 receptors in drug reward and conditioning. Two changes are consistently seen in addicted individuals: lower orbitofrontal/prefrontal function and fewer striatal dopamine D2 receptors. Understanding these neurobiological mechanisms gives a framework for better diagnosis, prevention and treatment of substance use disorders.

1.INTRODUCTION

Addiction is defined as a chronic, relapsing disorder characterized by compulsive drug seeking and use despite adverse consequences.[1] It is considered a brain disorder, because it involves functional changes to brain circuits involved in reward, stress, and self-control, and those changes may last a long time after a person has stopped taking drugs.[2] Addiction is a lot like other diseases, such as heart disease. Both disrupt the normal, healthy functioning of an organ in the body, both have serious harmful effects, and both are, in many cases, preventable and treatable. If left untreated, they can last a lifetime and may lead to death.

In general, people take drugs for a few reasons:

• To feel good. Drugs can produce intense feelings of pleasure. This initial euphoria is followed by other effects, which differ with the type of drug used. For example, with stimulants such as cocaine, the high is followed by feelings of power, self-confidence, and increased energy. In contrast, the euphoria caused by opioids such as heroin is followed by feelings of relaxation and satisfaction.

• To feel better. Some people who suffer from social anxiety, stress, and depression start using drugs to try to feel less anxious. Stress can play a major role in starting and continuing drug use as well as relapse (return to drug use) in patients recovering from addiction.

• To do better. Some people feel pressure to improve their focus in school or at work or their abilities in sports. This can play a role in trying or continuing to use drugs, such as prescription stimulants or cocaine.

• Curiosity and social pressure. In this respect, teens are particularly at risk because peer pressure can be very strong. Teens are more likely than adults to act in risky or daring ways to impress their friends and show their independence from parents and social rules.

2.BIOLOGICAL FACTORS INCREASE THE RISK OF ADDICTION

Biological factors that can affect a person's risk of addiction include their genes, stage of development, and even gender or ethnicity. Scientists estimate that genes, including the effects environmental factors have on a person's gene expression, called epigenetics, account for between 40 and 60 percent of a person's risk of addiction.[3] Also, teens and people with mental disorders are at greater risk of drug use and addiction than others.[4]

2.1. ENVIRONMENTAL FACTORS increase the risk of addiction

Environmental factors are those related to the family, school, and neighborhood. Factors that can increase a person's risk include the following:

• Home and family. The home environment, especially during childhood, is a very important factor. Parents or older family members who use drugs or misuse alcohol, or who break the law, can increase children's risk of future drug problems.[5]

• Peers and school. Friends and other peers can have an increasingly strong influence during the teen years. Teens who use drugs can sway even those without risk factors to try drugs for the first time. Struggling in school or having poor social skills can put a child at further risk for using or becoming addicted to drugs.[6]

other factors increase the RISK OF ADDICTION?

• Early use. Although taking drugs at any age can lead to addiction, research shows that the earlier a person begins to use drugs, the more likely he or she is to develop serious problems.[7] This may be due to the harmful effect that drugs can have on the developing brain.[8] It also may result from a mix of early social and biological risk factors, including lack of a stable home or family, exposure to physical or sexual abuse, genes, or mental illness. Still, the fact remains that early use is a strong indicator of problems ahead, including addiction.

How the drug is taken. Smoking a drug or injecting it into a vein increases its addictive potential .[9,10] Both smoked and injected drugs enter the brain within seconds, producing a powerful rush of pleasure. However, this intense high can fade within a few minutes. Scientists believe this starkly felt contrast drives some people to repeated drug taking in an attempt to recapture the fleeting pleasurable state.

3. PREVENTING DRUG MISUSE AND ADDICTION:

3.1.Why is adolescence a critical time for PREVENTING DRUG ADDICTION

As noted previously, early use of drugs increases a person's chances of becoming addicted. Remember, drugs change the brain— and this can lead to addiction and other serious problems. So, preventing early use of drugs or alcohol may go a long way in reducing these risks. Risk of drug use increases greatly during times of transition. For an adult, a divorce or loss of a job may increase the risk of drug use. For a teenager, risky times include moving, family divorce, or changing schools.[11] When children advance from elementary through middle school, they face new and challenging social, family, and academic

situations. Often during this period, children are exposed to substances such as cigarettes and alcohol for the first time. When they enter high school, teens may encounter greater availability of drugs, drug use by older teens, and social activities where drugs are used. A certain amount of risk-taking is a normal part of adolescent development. The desire to try new things and become more independent is healthy, but it may also increase teens' tendencies to experiment with drugs. The parts of the brain that control judgment and decision-making do not fully develop until people are in their early or mid-20s; this limits a teen's ability to accurately assess the risks of drug experimentation and makes young people more vulnerable to peer pressure.36 Because the brain is still developing, using drugs at this age has more potential to disrupt brain function in areas critical to motivation, memory, learning, judgment, and behavior control.[12] So, it's not surprising that teens who use alcohol and other drugs often have family and social problems, poor academic performance, health-related problems (including mental health conditions), and involvement with the juvenile justice system.

4. PARTS OF THE BRAIN ARE AFFECTED BY DRUG USE

Drugs can alter important brain areas that are necessary for life-sustaining functions and can drive the compulsive drug use that marks addiction. Brain areas affected by drug use include:

• The basal ganglia, which play an important role in positive forms of motivation, including the pleasurable effects of healthy activities like eating, socializing, and sex, and are also involved in the formation of habits and routines. These areas form a key node of what is sometimes called the brain's "reward circuit." Drugs over-activate this circuit, producing the euphoria of the drug high; but with repeated exposure, the circuit adapts to the presence of the drug, diminishing its sensitivity and making it hard to feel pleasure from anything besides the drug.

• The extended amygdala plays a role in stressful feelings like anxiety, irritability, and unease, which characterize withdrawal after the drug high fades and thus motivates the person to seek the drug again. This circuit becomes increasingly sensitive with increased drug use. Over time, a person with substance use disorder uses drugs to get temporary relief from this discomfort rather than to get high.

• The prefrontal cortex powers the ability to think, plan, solve problems, make decisions, and exert self-control over impulses. This is also the last part of the brain to mature, making teens most vulnerable. Shifting balance between this circuit and the reward and stress circuits of the basal ganglia and extended amygdala make a person with a substance use disorder seek the drug compulsively with reduced impulse control. Some drugs like opioids also affect other parts of the brain, such as the brain stem, which controls basic functions critical to life, such as heart rate, breathing, and sleeping explaining why overdoses can cause depressed breathing and death.

5. STAGES OF ADDICTION:

5.1. Binge and intoxication

All known addictive drugs activate reward regions in the brain by causing sharp increases in the release of dopamine.[13-15] At the receptor level, these increases elicit a reward signal that triggers associative learning or conditioning. In this type of Pavlovian learning, repeated experiences of reward become associated with the environmental stimuli that precede them. With repeated exposure to the same reward, dopamine cells stop firing in response to the reward itself and instead fire in an nticipatory response to the conditioned stimuli (referred to as "cues") that in a sense predict the delivery of the reward. [16] This process involves the same molecular mechanisms that strengthen synaptic connections during learning and memory formation . In this way, environmental stimuli that are repeatedly paired with drug use — including environments in which a drug has been taken, persons with whom it has been taken, and the mental state of a person before it was taken — may all come to elicit conditioned, fast surges of dopamine release that trigger craving for the drug[17] , motivate drug-seeking behaviors, and lead to heavy "binge" use of the drug. [18-20] These conditioned responses become deeply ingrained and can trigger strong cravings for a drug long after use has stopped (e.g., owing to incarceration or treatment) and even in the face of sanctions against its use.

6.2. Withdrawal and negative affect

An important result of the conditioned physiologic processes involved in drug addiction is that ordinary, healthful rewards lose their former motivational power. In a person with addiction, the reward and motivational systems become reoriented

through conditioning to focus on the more potent release of dopamine produced by the drug and its cues. The landscape of the person with addiction becomes restricted to one of cues and triggers for drug use. However, this is only one of the ways in which addiction changes motivation and behavior. For many years it was believed that over time persons with addiction would become more sensitive to the rewarding effects of drugs and that this increased sensitivity would be reflected in higher levels of dopamine in the circuits of their brains that process reward (including the nucleus accumbens and the dorsal striatum) than the levels in persons who never had a drug addiction. Although this theory seemed to make sense, research has shown that it is incorrect. In fact, clinical and preclinical studies have shown that drug consumption triggers much smaller increases in dopamine levels in the presence of addiction (in both animals and humans) than in its absence (i.e., in persons who have never used drugs).[19,20,21,22] This attenuated release of dopamine renders the brain's reward system much less sensitive to stimulation by both drug-related and non–drug-related rewards. [23-25] As a result, persons with addiction no longer experience the same degree of euphoria from a drug as they did when they first started using it. It is for this same reason that persons with addiction often become less motivated by everyday stimuli (e.g., relationships and activities) that they had previously found to be motivating and rewarding. Again, it is important to note that these changes become deeply ingrained and cannot be immediately reversed through the simple termination of drug use (e.g., detoxification)

6.3. Preoccupation and anticipation

The changes that occur in the reward and emotional circuits of the brain are accompanied by changes in the function of the prefrontal cortical regions, which are involved in executive processes. Specifically, the down-regulation of dopamine signaling that dulls the reward circuits' sensitivity to pleasure also occurs in prefrontal brain regions and their associated circuits, seriously impairing executive processes, among which are the capacities for self-regulation, decision making, flexibility in the selection and initiation of action, attribution of salience (the assignment of relative value), and the monitoring of error.[26] The modulation of the reward and emotional circuits of prefrontal regions is further disrupted by neuroplastic changes in glutamatergic signaling. [27] In persons with addiction, the impaired signaling of dopamine and glutamate in the prefrontal regions of the brain weakens their ability to resist strong urges or to follow through on decisions to stop taking the drug. These effects explain why persons with addiction can be sincere in their desire and intention to stop using a drug and yet simultaneously impulsive and unable to follow through on their resolve.

6. THE ROLE OF DOPAMINE IN ADDICTION:

Addictive drugs are inherently rewarding. They highjack the brain's dopamine system to increase dopamine levels in the nucleus accumbens, a key focal point for reward neurocircuitry in the brain. [28] While dopamine is critical for the rewarding effects of drugs, its role in substance use disorders is still evolving. Nearly 20 years ago, Nora Volkow (National Institute on Drug Abuse, National Institutes of Health) showed via positron emission tomography imaging that higher dopamine levels correspond with a more intense high in healthy volunteers given intravenous methylphenidate (MPH), a central nervous stimulant also known as Ritalin. There was considerable variability in dopamine levels across subjects; some individuals experienced neither increased dopamine levels nor "high." Administration of oral MPH, which takes longer to enter the brain, resulted in no high with slower increases in dopamine levels. 39 Since the rate of dopamine increase plays a factor in whether a drug will produce a rewarding effect, the different properties and effects of dopamine receptors in the brain are likely to play significant roles. The prefrontal cortex contains both dopamine D1 and D2 receptors. D2 receptors have an approximately 10- to 100-fold greater affinity for dopamine than D1 receptors and are therefore activated at lower dopamine concentrations. Under normal circumstances, the prefrontal cortex receives a low level, stable flow of dopamine owing to relatively slow, tonic firing of dopamine neurons in the ventral tegmental area (VTA) that project to the cortex. However, in response to an unexpected event, such as an extraordinary reward or very aversive event, dopamine neurons fire much more quickly. This phasic firing results in an abrupt, yet transient, increase in dopamine. The high levels of dopamine achieved during phasic firing are able to activate D1 receptors and are thought to be required for dopamine's full rewarding effects.[29,30] Drugs of abuse, particularly psychostimulants, mimic the high dopamine concentrations produced by phasic firing and thus activate both D1 and D2 receptors.[31] D1 receptors stimulate both reward, via pathways modulating the striatum and cortex, and conditioning and memory mechanisms that involve the amygdala, medial orbitofrontal cortex (OFC), and hippocampus. The conditioning/memory processes critical to addiction allows individuals to automatically associate a stimulus with a reward or punishment. Perhaps paradoxically, several studies have shown that addictive drugs fail to increase dopamine release in addicted individuals compared with non addicted controls.

7.SUMMARY AND CONCLUSIONS

Much progress in neurobiology has provided a useful neurocircuitry framework with which to identify the neurobiological and neuroadaptive mechanisms involved in the development of drug addiction. The brain reward system implicated in the development of addiction is composed of key elements of the basal forebrain with a focus on the nucleus accumbens and central nucleus of the amygdala. Neuropharmacological studies in animal models of addiction have provided evidence for the activation of specific neurochemical mechanisms in specific brain reward neurochemical systems in the basal forebrain (dopamine, opioid peptides, GABA, and endocannabinoids) during the binge/ intoxication stage. During the withdrawal/ negative affect stage, dysregulation of the same brain reward neurochemical systems occurs in the basal forebrain (dopamine, opioid peptides, GABA, and endocannabinoids). There is also recruitment of brain stress/aversion systems (CRF and dynorphin) and dysregulation of brain antistress systems (neuropeptide Y) that contribute to the negative motivational state associated with drug abstinence. During the preoccupation/ anticipation stage, neurobiological circuits that engage the frontal cortex glutamatergic projections to the nucleus accumbens are critical for drug-induced reinstatement, whereas basolateral amygdala and ventral subiculum glutamatergic projections to the nucleus accumbens are involved in cue-induced reinstatement. Stress-induced reinstatement appears to be mediated by changes in the antireward systems of the extended amygdala. The changes in craving and antireward (stress) systems are hypothesized to remain outside of a homeostatic state, and as such convey the vulnerability for the development of dependence and relapse in addiction. Genetic studies to date in animals suggest roles for the genes encoding the neurochemical elements involved in the brain reward (dopamine, opioid peptide) and stress (neuropeptide Y) systems in the vulnerability to addiction. Molecular studies have identified transduction and transcription factors that may mediate the dependence-induced reward dysregulation (CREB) and chronic-vulnerability changes (ΔFosB) in neurocircuitry associated with the development and maintenance of addiction. Human imaging studies reveal similar neurocircuits involved in acute intoxication, chronic drug dependence, and vulnerability to relapse. Although no exact imaging results necessarily predict addiction, two salient changes in established and unrecovered substance-dependent individuals that cut across different drugs are decreases in orbitofrontal/prefrontal cortex function and decreases in brain dopamine D2 receptors. No molecular markers are sufficiently specific to predict the vulnerability to addiction, but changes in certain intermediate early genes with chronic drug exposure in animal models show promise of long-term changes in specific brain regions that may be common to all drugs of abuse. The continually evolving knowledge base of the biological and neurobiological aspects of substance use disorders provides a heuristic framework to better develop diagnoses, prevention, and treatment of substance abuse disorders.

REFRENCES:

[1] National Drug Intelligence Center. The economic impact of illicit drug use on American society. Washington, DC: United States Department of Justice, 2011.
[2] Goldstein RZ, Volkow ND. Dysfunction of the prefrontal cortex in addiction: neuroimaging findings and clinical implications. Nat Rev Neurosci. 2011;12(11):652-669. doi:10.1038/nrn3119
[3] Bevilacqua L, Goldman D. Genes and addictions. Clin Pharmacol Ther. 2009;85(4):359-361. doi:10.1038/clpt.2009.6
[4] Substance Abuse and Mental Health Services Administration. Mental and Substance Use Disorders. https://www.samhsa.gov/ disorders. Published June 20, 2014. Accessed June 4, 2018.
[5] Biederman J, Faraone SV, Monuteaux MC, Feighner JA. Patterns of alcohol and drug use in adolescents can be predicted by parental substance use disorders. Pediatrics. 2000;106(4):792-797. 6. Whitesell M, Bachand A, Peel J, Brown M. Familial, social, and individual factors contributing to risk for adolescent substance use. Journal of Addiction. https://www.hindawi.com/journals/ jad/2013/579310/. Published 2013. Accessed June 4, 2018
[6] Substance Abuse and Mental Health Services Administration. Mental and Substance Use Disorders. https://www.samhsa.gov/ disorders. Published June 20, 2014. Accessed June 4, 2018.
[7] Lynskey MT, Heath AC, Bucholz KK, Slutske WS, Madden PAF, Nelson EC, Statham DJ, Martin NG. Escalation of drug use in earlyonset cannabis users vs co-twin controls. JAMA 289: 427-33, 2003.
[8] Squeglia LM, Jacobus J, Tapert SF. The influence of substance use on adolescent brain development. Clin Neurosci Soc ENCS. 2009;40(1):31-38.
[9] Verebey K, Gold MS. From coca leaves to crack: the effects of dose and routes of administration in abuse liability. Psychiatr Annals 18:513–520, 1988.

[10] Hatsukami DK, Fischman MW. Crack cocaine and cocaine hydrochloride: Are the differences myth or reality. JAMA 276:1580-1588, 1996
[11] Fowler JS, Volkow ND, Kassed CA, Chang L. Imaging the addicted human brain. Sci Pract Perspect 3(2):4-16, 2007.
[12] Di Chiara G. Nucleus accumbens shell and core dopamine: differential role in behavior and addiction. Behav Brain Res 2002;137:75-114
[13] Koob GF. Neural mechanisms of drug reinforcement. Ann N Y Acad Sci 1992;654:171-191
[14] Wise RA. Dopamine and reward: the anhedonia hypothesis 30 years on. Neurotox Res 2008;14:169-183
[15] SchultzW.Gettingformalwithdopamine and reward. Neuron 2002;36:241-263
[16] VolkowND,WangGJ, TelangF, et al. Cocaine cues and dopamine in dorsal striatum:mechanismofcravingincocaine addiction. J Neurosci 2006;26:6583-6588
[17] Weiss F. Neurobiology of craving, conditionedrewardandrelapse. CurrOpin Pharmacol 2005;5:9-19 .VolkowND,WangGJ,Fowler JS, et al. Decreased striatal dopaminergic responsiveness in detoxified cocaine-dependent subjects. Nature 1997;386:830-833
[18] Zhang Y, Schlussman SD, Rabkin J, ButelmanER,HoA,KreekMJ.Chronic escalating cocaine exposure, abstinence/withdrawal, and chronic re-exposure: effects on striatal dopamine and opioid systems in C57BL/6J mice. Neuropharmacology 2013;67:259-2 66.
[19] MüllerCA,GeiselO,BanasR,HeinzA. Current pharmacological treatment approaches for alcohol dependence. Expert Opin Pharmacother 2014;15:471-481
[20] VolkowND, TomasiD,WangGJ, et al. Stimulant-induceddopamineincreasesare markedly blunted in active cocaine abusers. Mol Psychiatry 2014;19:1037-1043
[21] HägeleC,SchlagenhaufF,RappM,etal. Dimensional psychiatry: reward dysfunction anddepressivemood across psychiatric disorders. Psychopharmacology (Berl) 2015;232:331-341
[22] Hyatt CJ, Assaf M, Muska CE, et al. Reward-related dorsal striatal activity differences between former and current cocaine dependent individuals during an interactive competitive game. PLoS One 2012;7:e34917-e34917
[23] KonovaAB,MoellerSJ,TomasiD,etal. Structural and behavioral correlates of abnormalencodingofmoneyvalueinthe sensorimotor striatum in cocaine addiction. Eur J Neurosci 2012;36:2979-2988
[24] GoldsteinRZ,VolkowND.Dysfunction of the prefrontal cortex in addiction: neuroimaging findings and clinical implications. Nat Rev Neurosci 2011;12:652-669
[25] Britt JP, Bonci A. Optogenetic interrogations of the neural circuits underlying addiction. Curr Opin Neurobiol 2013;23:539-545
[26] Volkow, N.D., G.-J. Wang, J.S. Fowler, et al. 2011. Addiction: beyond dopamine reward circuitry. Proc. Natl. Acad. Sci. USA 108: 15037– 15042.
[27] Grace,A.A. 2000. Thetonic/phasicmodel of dopamine system regulation and its implicationsforunderstandingalcoholand psychostimulant craving. Addiction 95(Suppl. 2): S119– S128.
[28] Baik, J.-H. 2013. Dopamine signaling in reward-related behaviors. Front. Neural Circuits 7: 152.
[29] Volkow, N.D. & M. Morales. 2015. The brain on drugs: from reward to addiction. Cell 162: 712– 725.