

The Science of Addiction: Neurobiological Perspectives

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ABSTRACT

Addiction is a complex and chronic disorder characterized by compulsive substance use or engagement in behaviors despite adverse consequences. This paper offers a comprehensive overview of addiction through a neurobiological lens, integrating historical developments, genetic and environmental influences, psychological factors, and treatment paradigms. Emphasizing addiction's biological roots, especially within brain reward circuits such as the nucleus accumbens and prefrontal cortex, it explores how neural adaptations contribute to compulsivity and relapse. The interaction between genetic predispositions, environmental stressors, and psychosocial triggers is also examined to explain individual vulnerability. Additionally, the paper discusses behavioral addictions and the implications of digital technologies on addictive patterns. Highlighting treatment challenges and the necessity for interdisciplinary approaches, it argues for more holistic and globally coordinated responses. This review underscores the need to bridge biological science with social understanding to enhance prevention, diagnosis, and rehabilitation in addiction science.

Keywords: Addiction, Neurobiology, Brain Reward Circuitry, Substance Use Disorders, Genetic Vulnerability, Environmental Stressors, Behavioral Addiction, Adolescent Risk.

INTRODUCTION

Drug addiction is the compulsive seeking and taking of drugs despite negative consequences. This disorder involves long-lasting brain changes that affect reinforcement and cognitive control. Drugs create neuroadaptations that enhance drug-related signals, causing the brain to be more responsive to drugs than to natural rewards. Vulnerability to addiction arises from genetic and environmental factors. Genetic elements, such as polymorphisms and copy number variations, account for around 50% of the risk, while environmental influences include prenatal toxin exposure, parenting styles, peer pressure, and direct drug exposure. Understanding the biology of addiction, particularly the role of the nucleus accumbens and other brain circuits, is essential. Some individuals show increased vulnerability to social and psychological influences that drive drug-seeking behavior. Factors like drug availability, peer dynamics, and stress can raise addiction risks by making certain individuals more sensitive. Research has revealed that those with prior drug exposure or stress histories are likelier to self-administer drugs. Studies have led to insights into the neurobiological mechanisms underlying heavy drug consumption and how individual differences shape the brain circuits involved in reinforcement processing [1, 2].

Historical Overview of Addiction Research

Classical versions of the symptomatology of substance use disorders have documented the wide variation in onset, course, specific symptoms, and long-term outcomes of addiction. However, chronic drug use results in a relatively common and concerning syndrome characterized by escalation of intake to the point where substance use overtakes all other interests; persistence of use despite well-articulated negative consequences; a cross-generational and cross-population vulnerability to this syndrome; and a plethora of beliefs and/or behaviors regarding substance use that are impervious to evidence (plausible deniability and cognitive dissonance). Informal observations also reveal a spectrum of severity of substance use disorders. The above considerations highlight the need for a more mechanistic-level approach and why

transgenic animals were originally developed for the study of the possible pathophysiology of substance use disorders. Research on the neurobiological basis of addiction has been carried out since the advent of drug self-administration in the mid-1950s. Much early work focused on the motivational properties of drugs for learning and reinforcement, but also on the behavioral syndrome displayed in addiction. The forward movement of research on the underpinnings of addiction accelerated in the early-to-mid-1990s with the advent of neurobiological systems-level approaches to the mammalian brain. The integration of neuroanatomy with neurochemical and neuropharmacological techniques made it feasible to begin exploring the neurobiological basis of the early and long-term consequences of various classes of drugs of abuse and how these consequences may be related to the dynamics of the behavioral syndrome displayed by addiction. In particular, the rapidly evolving fields of neuropharmacology, neurochemistry, and gene regulation have provided, and will continue to provide, tools suitable for addressing these issues [3, 4].

Neurobiological Basis of Addiction

Addiction is a disorder that arises from the interaction among the properties of the drug, the individual's neurobiology, and the social environment. Thus, addiction is profoundly social, and social influences on vulnerability to addiction can be at least partly understood from a neurobiological perspective. With the recent advancements in neural imaging techniques, there is now a robust understanding of the neurobiology of addiction. Individual brain imaging variables cannot be thought of in isolation, as they are being processed by the same neural circuitry. Collectively, these inputs drive action selection and the execution of behavior, say, to drink or not to drink, and then, within an episode, to stop drinking or keep drinking. Modern addiction science is an interdisciplinary enterprise. It involves inputs from neuroscience, genetics, pharmacology, theories of behavior, epidemiology, economics, and sociology. In recent years, the scientific understanding of addiction has made remarkable strides, particularly in the neurobiological domain. Much had been learned about the brain neuroadaptations, biological factors, and neurobiological mechanisms that underlie the compulsive use of the drug, repeated relapse, or other hallmarks of addiction. Among the properties of a drug, its pharmacological action on target receptors is a fundamental consideration. Nonetheless, reports on how social factors penetrate and, in turn, influence neural processing in the context of addiction are starting to appear. While brain-centric accounts of addiction emphasize neurobiology, neurocircuitry, and molecular biology, they have not paid enough attention to the inputs that social factors provide to neural processing behind drug seeking and taking. They have also missed that neural circuitry for social processes and effects of social environments on brain function and behavior are key foci within neuroscience, ethology, and psychology [5, 6].

Genetics and Addiction

Genetics influence vulnerability or resilience to drug addiction, interacting with environmental factors, and are regulated epigenetically. Most people use psychoactive substances occasionally without issues, but a minority develop compulsive habits, termed addiction. This chronic disorder often becomes progressive and is marked by relapse; thus, while some become addicted, most do not. Only a small fraction of users abuse drugs, which refers to usage that causes distress or impairment. Given that addiction represents a severe form of substance use disorder, estimated rates of addiction (2%-8%) are lower than total use disorders (15%-40%). Addiction exists on a spectrum from benign use to misuse, abuse, and ultimately addiction. This progression is nonlinear; for most, misuse is temporary, but for others, it can become chronic or relapsing due to fluctuations related to affect dysregulation, essentially, changing emotional responses to drug use. Genetics significantly contribute to addiction risk. Understanding the neurobiological mechanisms behind addiction is crucial. Genetic animal models serve as powerful tools to analyze vulnerability to addiction, and familial trends suggest a genetic component, supported by twin studies. Research has focused on addiction phenotypes within animal models. These laboratories offer advantages such as brain manipulation, genetic analysis, and cost-effectiveness. Two strategies in this research include selective breeding and using diverse strains. However, rodent models are polygenic, complicating the identification of underlying genetic variants. Comprehensive genotyping and phenotyping have been done, yet connecting genetic differences to neurobiology remains challenging due to the diversity in genetic divergence. Exploring broader models of addiction pathways may prove more insightful, as they are central to how drugs affect synaptic transmission and plasticity, thereby influencing addiction mechanisms. Understanding these alterations can enhance insight into addiction [7, 8].

Psychological Factors in Addiction

Human involvement with psychoactive substances spans thousands of years across various cultures, often emphasizing the associated harms. Over the past century, societies have implemented measures to regulate use, yet the prevalence of substance use disorders (addiction) has increased, coinciding with the rising availability of these substances. Psychoactive substances are a significant human invention, akin to the discovery of fire, representing both expression and struggle. Although the negative impacts are frequently highlighted, these substances also provide societal benefits and are complex compounds developed over millennia. Recent advancements in understanding addiction have revealed neurobiological mechanisms linked to its compulsive nature. Since the 1990s, evidence shows that addiction correlates with structural and functional brain changes, particularly in reward, attention, memory, and motivation, with genetic predisposition playing a role. Research indicates a reciprocal relationship between these neurobiological deficits and addiction, shaping a new perspective among clinicians regarding those affected. Meanwhile, insights from Nobel laureates have reframed addiction as a coping mechanism, where individuals use psychoactive substances to manage distress. This coping-oriented approach holds a paradox: while substances may temporarily alleviate mental pain, excessive use often exacerbates suffering, which, despite the diversity of substances, remains fundamentally similar across different individuals [9, 10].

Environmental Influences on Addiction

As discussed in Section 4, in addition to differences in genes, the environment plays an important role in influencing an individual's propensity to become an addict. Environmental influences on the propensity for addiction are broad in scope, but the scientific community is primarily interested in three types of environmental factors: exposure to a drug of abuse, environmental stress and trauma, and social isolation and deprivation. About drug exposure, generally, preclinical studies show that a prolonged or intense drug exposure considerably increases the likelihood that an animal subsequently will self-administer that drug. In humans, an important consideration is gateway drugs, relatively innocuous drugs, but that increase the likelihood of use of other, more harmful or addictive drugs. Drugs such as alcohol, nicotine, and marijuana are of particular concern in this regard. Secondly, environmental stresses, traumas, and other harsh experiences, such as allyship or neglect during parenting, also increase the likelihood of later addiction. Finally, environmental enrichment and social integration are protective against addiction, while social isolation, peer pressure, or a scarcity of important social relationships increase the risk. Further research in these areas will deepen the understanding of the development of addiction and prognosis with treatment. Given the severe health, social, and economic costs of addiction, the public health implications for society are enormous. It is realized, however, that there likely are broad societal differences in the degree to which research knowledge is applied to programs of education, prevention, and treatment. These issues of societal implementation present challenges that are perhaps even greater than those of the biological sciences [11, 12].

Addiction across the Lifespan

Addiction is a chronic disease impacting many, with recent focus on its neurobiology. Gene-environment interactions can alter brain structure and chemistry, leading to compulsive behaviors. Studying addiction across the lifespan is essential for understanding its causes and progression. Advances in genetic, epigenetic, and pharmaceutical interventions offer important opportunities for improved prevention and treatment. Adolescents have unique neurobiological characteristics that aid in understanding drug abuse. Significant changes in reward circuitry during this period heighten responsiveness to drugs and natural rewards, promoting risk-taking and impulsivity typical of adolescence. While many adolescents experiment with substances, some face abuse and dependence, resulting in health issues. Recognizing the impact of drug use on the adolescent brain is crucial, especially during this complex developmental stage. As neural connections mature, behavioral changes arise, characterized by heightened risk-taking and sensation-seeking. Investigating reward mechanisms in adolescents highlights the overlap in neurobiological functions related to incentive and pleasure, indicating that increased activation in these areas contributes to typical adolescent behaviors. Notably, high sensation-seeking and impulsivity predict future drug addiction risk. Adolescents displaying these traits face the highest likelihood of developing addiction. Exploring the connections between these traits and adult addiction profiles will guide future research efforts [13, 14].

Substance Use Disorders

Substance use disorders (SUDs) affect around 20 million people per year in the United States alone. SUDs are conditions that are characterized by a pattern of hazardous use of psychoactive substances resulting in significant impairment, distress, and problems. The most exacerbating factor for the development of SUDs is trauma exposure, such as childhood maltreatment or adult sexual assault. However, although both traumatic exposure and SUDs are prevalent and related conditions, the underlying mechanisms of this relation remain poorly understood. Importantly, these disorders are often co-occurring. Many individuals who are exposed to trauma do not develop a SUD, yet for others, substances become a maladaptive way of coping with the trauma. Given how prevalent and impairing both alcohol-use disorders and PTSD are, understanding the mechanisms of their interactions represents an important clinical and public health problem. Given that trauma and early-life stress cascade-associated neurobiological alterations involve systems that are known to be implicated in substance use, the reward circuitry, negative emotionality, and inhibition, it is posited that they may be key pathways through which trauma exposure influences the risk of hazardous substance use. A scatter of literature has explored the relation among SUDs, trauma, and neurobiology; however, to the best of the authors' knowledge, there is currently no systematic review comprehensively covering the neurobiological alterations associated with both SUDs and trauma exposure, while also offering insights on domains to guide future research. Moreover, while there is no systematic review linking the SUDs and the neurobiological underpinnings of trauma exposure, several neuroimaging studies have investigated the associations of these conditions separately. Interestingly, the neuroimaging literature covers neural alterations across brain regions involved in the SUD-related constructs of reward, negative emotionality, and inhibition. This stark difference across the two domains of SUDs and trauma suggests that SUDs may be neomorphic or in some other way different or distinct from other disorders [15, 16].

Behavioral Addictions

In addition to substance addiction, behavior addictions are increasingly investigated due to technological developments such as the internet. Depending on current definitions of addiction, behavioral problems specifically brought on by gambling, gaming, sex, shopping, and compulsive internet use may or may not be broadly classified as behavioral addictions. However, as behavioral addictions raise similar neurobiological issues as substance addictions, behavioral addictions are described here concerning how they inform the science of addiction through animal research. Problem gambling behavior became a public health problem this past decade due to the proliferation of gambling venues and gambling opportunities introduced through technological developments, especially the growth of the internet. The internet provided a vehicle for gambling expansion that contrasted with traditional forms of gambling availability, which required a substantial time commitment by individuals who limited gambling or prevented it completely. Whether these venues for gambling through the internet would produce substantially more problem gambling was questioned, but international epidemiology studies regarding internet gambling revealed the detrimental consequences of the advent of these technologies. Consequently, similar technologies for other activities or behaviors previously considered purely entertainment or recreation, such as video gaming, also became suspected of causing behavioral addictions like problem gambling. Similar queries for these technology-led problems were subsequently submitted to this research area despite the substantial differences in possible problematic consumptions. An analogous research framework was established regardless of convergence on the general term of "behavioral addictions." Treatment of either substance or behavioral addictions was thought to be directed or informed by a common basic understanding of addiction through scientific research, especially through comparisons and contrasts. However, substantive scientific comparisons or bases also left this area in the dark, causing soaring confusion among these similarities and differences, treating behavioral problems differently from substance problems [17, 18].

Treatment Approaches for Addiction

Patients with SUDs seek out, consume, and continue to consume a drug despite its demonstrated adverse consequences. Such behaviors present a real and pervasive public health concern globally. For this reason, how to best treat this disease has become one of the priorities of modern medicine. Yet, it remains a difficult question since the right approach to treatment is often dictated by the drug of abuse and the individual in need of treatment. There is a wide variety of pharmacotherapies available to treat SUDs,

each occupying a different position on the spectrum of treatment indication and use. The use, misuse, and abuse of potentially addictive drugs are certainly matters of public health. As such, they require the attention and resources of public health authorities at all levels of government. Addiction is a lifelong disorder that can be treated but cannot be cured completely. At present, less than 10% of individuals with addiction receive treatment, and a much lower proportion receive evidence-based treatment. Understanding and addressing the gaps in treatment, hoping to eliminate illegal drugs, relieve human suffering, and substantially reduce drug-related crime, is receiving much attention at all levels of the public and private sectors in most parts of the world. Despite a very concerted global interest in the problem and its consequences, international laws and conventions banning certain of the most potent addictive (and in many cases, deadly) drugs remain largely ineffective and widely ignored. With an ever-increasing abundance of such commodities becoming available at a much lower cost, meeting the public health challenge of addiction prevention, treatment, and control is certainly a demanding one. World-class state-of-the-art basic knowledge and technologies across all relevant fields are essential but insufficient unless innovative socio-political frameworks and public policies are devised and adopted globally. Such a monumental end goal may be a very difficult challenge to undertake. Nonetheless, many intermediate steps can be taken in addressing the problem of addiction and its treatment [19, 20].

Preventive Strategies in Addiction

Preventive Strategies in Addiction can be divided into opportunities to improve health data with adolescents and with an essential focus on neurological aspects. The fact that adolescents are particularly sensitive to external influence in both cognition and behavior gives them opportunities, but also renders preventive strategies more challenging. During that developmental period, better access to health data is considered to give the young the possibility to know and understand the risk of anthropogenic changes towards less health and expectancy of a better life, without the obvious attempt to condemn anyway the pleasures and virtuous satisfactions associated with sports and leisure. Consumption considered as addictive enhances not only yearn and craving (and thus negative affections), but also culinary/pharmaceutical life-cycle accountability problems that challenge everything related to guilt (therefore worse-quality products), and that alas may end up considered a regular or habitual consumption, and optimal lifestyle that should be enjoyed instead of controlled and aware of. Better preventives would encompass and consider that curiosity and intelligence itself come in its turn with risk, and that drugs do offer truly increased chances of tremendous, wonderful human experiences. Such concepts express far better than expected the odd nature of (preventive) impacts, which ought to be considered mildly better than bluntly imposed and then completely nullified. On a different level, and using such and more such information for a two hourly workshops when schools and programs are embattled with considering something there attractive enough for attendees and approvable in scientific terms, computer games simulating life directly from neurons, branched physically, differently connected, and variation possibilities of astrocytes synchronized by gap-junctions, considering dopaminergic ones that, avoiding unwanted presses should come back with almost intact other activated ones, both releasing and degrading motions, gradually assuring its activation or deactivation chances should be a second chance; self-married and engrossed supervision of coalescence of CRH release on basal (and reward) shoot-ups when distressed reconvenient neurons, despite immense wait hours, do boil life science down to dignity levels, and sympathy rather than race emulation; easy switches between reward, intoxication and sedative clades should leave and proper winning and luxurious clones losers should enable to feel too proud to search sympathy at expense of solidarity, or dialogue at the expense of continuously entertained excitement over loose talk, as recently attempted in another piece about alternative life-cycles embedded thoughts [21, 22].

Future Directions in Addiction Research

Despite tremendous advances in understanding the molecular and cellular adaptations that occur in brain reward regions in response to repeated exposure to a drug of abuse, many questions remain regarding the neurobiology of addiction. Understanding how drugs hijack the brain's reward circuitry to reinforce compulsive drug-seeking and drug-taking is one of the most important challenges facing neuroscience. Reward-related learning and memory paradigms should prove to be particularly useful vehicles for the understanding of the neurobiology of addiction since drugs of abuse produce a robust, long-lasting enhancement in the ability of reward-predictive cues to trigger craving for the drug and to reinstate

drug-seeking behavior. The continual adaptation of this circuitry to the presence of addictive drugs produces a set of negative reinforcement neurobiological adaptations to withdraw from their effects. Dramatic increases in craving upon cessation of use and re-exposure to drug-associated cues or contexts point to a set of positive reinforcement neuroadaptations that increase the saliency of drug-predictive cues or contexts. Many rewarding stimuli (natural and drug) engage overlapping sets of brain structures, including the mesolimbic dopamine system, which largely consists of striatal medium spiny projection neurons that release the neurotransmitter GABA. These brain areas and circuits have long been linked to addiction. Key components of addiction models continue to provide insights into facets of addiction, but key challenges remain for the field. Traditional neurobiological models of addiction regard the use of drugs as a homogenous and pathological behavior. Understanding the neurobiology of addiction requires moving beyond these models and taking into account the deconstruction of addiction, its modular nature, and system-wide analysis of the large-scale brain changes associated with addiction. Developing and optimizing diverse novel methodologies, particularly multisite neuronal recording techniques allied to sophisticated computational techniques, will be crucial in the understanding of how addictive drugs compromise goal-oriented behavior and learning, and give rise to compulsive disorderly use of the drug. Ultimately, this new knowledge will be essential in the identification of treatment targets and in the development of new therapies for conditions of abnormal drug taking, either as induction of orderly use or as treatment [23, 24].

Ethical Considerations in Addiction Research

This section does not explicitly address ethical concerns in contemporary addiction research, yet issues from prior commentary can be identified. Dominant themes include data from studies involving chronic recreational users of psychoactive drugs on non-testing days. "Chronic recreational users" refers to university students who spend significant discretionary funds on binge drinking, amphetamines, or heroin during earlier ichthyological training, many of whom now lead prestigious academic labs. If such research becomes an in-house joke, several problems arise. Anecdotal evidence suggests that academic addiction researchers often oppose drug law reform, reflecting a tendency to envision a "correct" world rather than addressing actual conditions. Another issue is the belief that positive drug research outcomes can be countered by theoretical frameworks supporting drug bans. Research since the 1970s shows this discrepancy. An academic's drug-free test day may disconnect them from the realities of chronic users, suggesting contemporary research often resembles mere replication rather than illuminating truths about addiction. Conflicting experimental outcomes are common, and addiction research is fraught with inaccurate predictive models. Despite claims of precision, the scrutiny of rich data reveals underlying issues. Notably, "science" and "scientific" are not synonymous, leaving no straightforward means to verify a science's openness or accuracy [25-28].

CONCLUSION

Addiction, whether to substances or behaviors, is a multifaceted disorder rooted in dynamic interactions between neurobiological, psychological, genetic, and environmental factors. Advances in neuroscience have illuminated how addiction alters brain function, particularly in regions involved in motivation, memory, and impulse control. However, the science of addiction cannot be confined to neurobiology alone. Social environment, trauma exposure, and developmental stages like adolescence significantly influence addiction trajectories. Genetic predispositions further complicate this picture, indicating a need for individualized and context-aware interventions. Despite scientific progress, major gaps persist in treatment accessibility, effectiveness, and implementation of evidence-based approaches. Tackling addiction requires not only cutting-edge research but also innovative public policies and cross-sector collaboration. Ultimately, understanding addiction from a neurobiological perspective, while incorporating social and psychological dimensions, offers the most promising path toward comprehensive care and effective prevention strategies.

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