

Unraveling the Complexities of Addiction: From Neurobiology to Social Determinants

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Abstract

Substance use disorders (SUDs) present a significant public health challenge globally, with profound consequences on individuals and society. The goal of this study is to better understand the complexities of addiction by looking at the interactions between neurobiology, neurotransmitter systems, and addictive behaviors. The research also highlights the difficulties in obtaining treatment and the discrepancies in care while discussing the effects of addictive behaviors on neurocognitive processes and understanding of illness.

Keywords: Substance Use Disorder, addiction, cravings, treatment, interventions.

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Chapter 1: Introduction

Addiction, the most severe form of substance use disorder (SUD), “is a chronic brain disorder molded by strong biosocial factors that have devastating consequences to individuals and society” (Volkow & Boyle, 2018). SUDs constitute a serious threat to public health not only in the United States but globally, with far-reaching economic, medical, and social consequences. The United States National Survey on Drug Use and Health (NSDUH) for 2022 reports that 16.7% of Americans, or 46.8 million people aged 12 and older, battled a substance use disorder in the previous year. In the previous year, 10.5% of Americans aged 12 and over suffered from an Alcohol Use Disorder (AUD) (*Alcohol and Drug Abuse Statistics*).

In the United States, the issue of drug use and abuse persists, and that is because of the complex nature of the issue. In order to understand the complexity of the issue, there must be a multifaceted approach that explores the medical, social, and legal dimensions. In the realm of neuroscience and addiction research, understanding the intricate interplay between neurobiological mechanisms, addictive behaviors, and neurotransmitter systems is crucial to unraveling the complexities of drug addiction.

Research Questions

This paper aims to examine the neurobiological mechanisms that contribute to the development and maintenance of addiction, particularly in the context of using hard drugs such as cocaine, heroin, and opioids. This paper will examine these neurobiological mechanisms to gain a deeper understanding of the complex interplay between addiction, neurocognitive functions, and neurotransmitter systems. In addition to that, this paper will explore how addictive behaviors affect neurocognitive functions such as decision-making, impulsivity, and cognitive control. Finally, this paper will investigate the impact of substance addiction on neurotransmitter

systems, including dopamine, serotonin, and glutamate, and how this contributes to the reinforcing nature of addictive behaviors. This knowledge can inform the development of more effective prevention and treatment strategies for individuals struggling with addiction.

Overview of Study

Secondary research of articles and books was used to obtain evidence relating to drug addiction and neuropsychology and the studies that correspond to it. The thesis will adopt a literature review format to delve into the multifaceted relationship between neuropsychology, addiction, and neurotransmitters. Each source was analyzed and contrasted with the others to obtain a more decisive idea about what effects addictive drugs have on humans in a holistic manner.

Purpose of the Study

This research is driven by the urgent need to deepen our comprehension of addiction mechanisms, especially concerning opioids, given their pervasive impact on individuals and society. By elucidating these complex relationships, the study aims to contribute valuable insights to inform evidence-based interventions and policies.

Field/Significance of the Study

The significance of this study lies in its potential to advance scientific understanding in the study of addiction. By bridging gaps in knowledge surrounding neurobiology, addictive behaviors, and neurotransmitters, this thesis seeks to pave the way for more targeted interventions, improved treatment approaches, and, ultimately, a positive impact on public health outcomes.

Definitions

Substance Use Disorder (SUD): "a maladaptive pattern of substance use, leading to clinically significant impairment or distress." (Sher & Trull, 2002)

alcohol use disorders (AUD): “**alcohol abuse** and **alcohol** dependence” (Maisto & Saitz, 2003)

Diagnostic and Statistical Manual of Mental Disorders (DSM) (Vafaie & Kober, 2022).

Post-Traumatic Stress Disorder (PTSD) “It is a psychiatric disorder that may occur in people who have experienced or witnessed a traumatic event, series of events or set of circumstances”.

(<https://www.psychiatry.org/patients-families/ptsd/what-is-ptsd>)

Limitations

It is important to note that with only Anna Maria databases, much of the information was unavailable. Often, articles would appear that focused on the narrow topic needed, but without access, there was no way to gather that data. With limited sources and time, the plethora of information was constricted. However, significant gaps remain in our scientific understanding of the neurobiological underpinnings of addiction. Key questions persist around the interplay between genetic, environmental, and neurological factors that contribute to the onset and progression of substance use disorders. Elucidating these complex relationships is essential for developing more effective prevention strategies and personalized treatment approaches.

Chapter 2: Methodologies

For this thesis, research articles and books were read and synthesized to comprise an analysis of the complex relationship between neurobiological mechanisms, addictive behaviors, and neurotransmitter systems in order to comprehend the complexity of Substance Abuse disorders. The databases used were SocINDEX with Full Text, Gale Onefile Psychology, and Google Scholar. Books written by academic scholars available in the bookstore were the source of all books except one. One book was found through a course on Addiction that I took the same semester I conducted my thesis.

While going through these sources, search terms such as "drugs," "opioid crisis," "neurobiological mechanisms," "impact," "addiction," "opioid crisis," "neurobiological," "neurotransmitters," and "opioid" were included in different combinations (See Appendix Figure 1: Methods Chart). Exclusion criteria included all articles published before 2000, as well as those that were not peer-reviewed, not in English, and not fully described by Anna Maria College. Thus, only articles after 2000 that were full-text, peer-reviewed, and in English were reviewed. There were no strict exclusions on sample size as this topic is relatively new, and some data can be limited, especially when it comes to special populations.

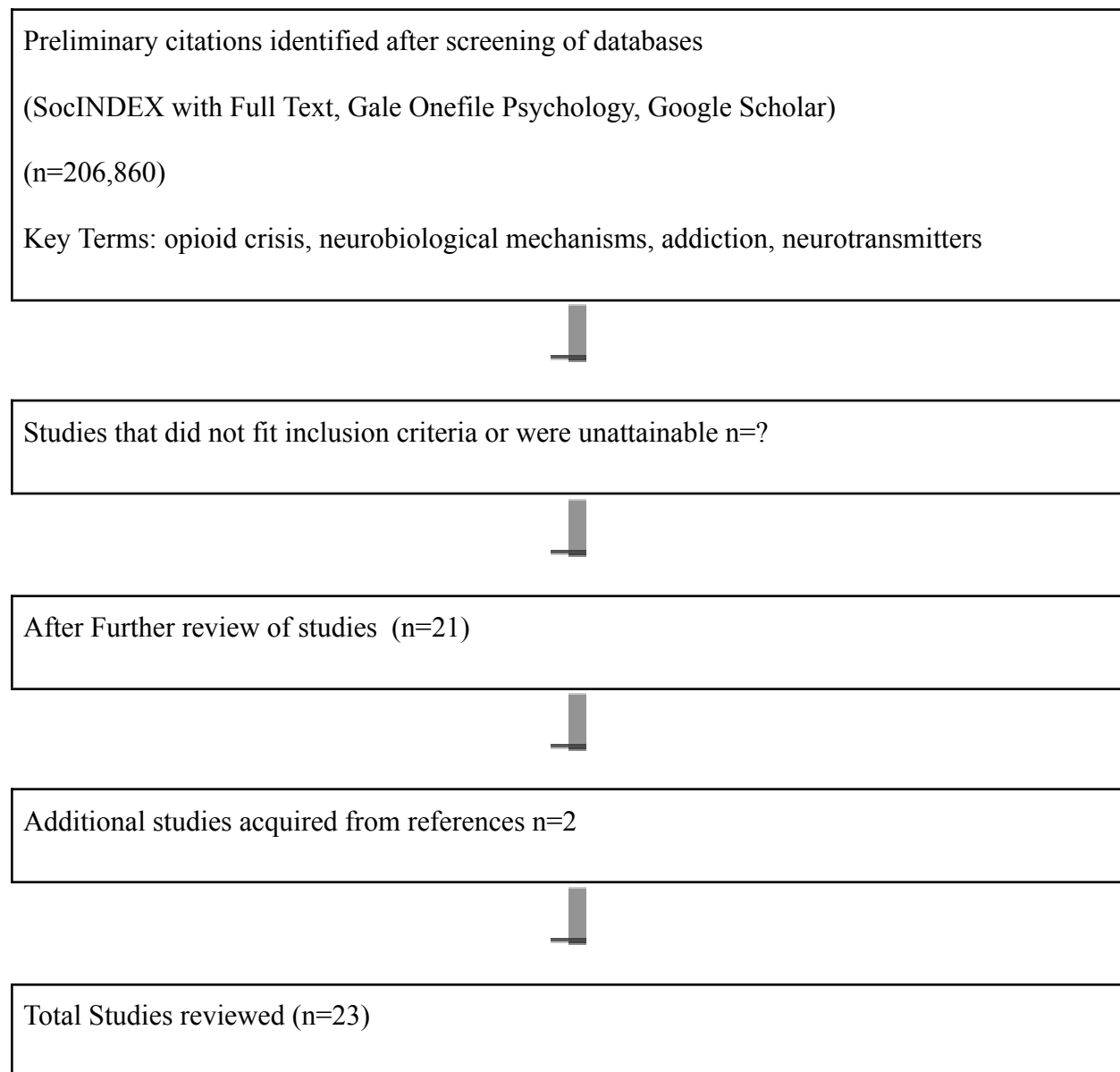
The initial search yielded 206,860 results, but after exclusion information was used, 206,837 sources were cut out. The remaining number is 23 sources. The first few pages of those 23 sources were then skimmed by title and year. Only 21 articles corresponded to my topic from the databases SocINDEX with Full Text, Gale Onefile Psychology, and Google Scholar. One book was found from a different course I took at Anna Maria, and the other was found from popular books. These 2 sources were included in this literature review.

The articles and books were critically analyzed and compared in relation to one another and the overall topic of understanding the complex relationship between neurobiological mechanisms, addictive behaviors, and neurotransmitter systems in order to comprehend the complexity of Substance Abuse Disorders. The study's research methodology had the advantage of focusing on a particular subject and giving access to a wide selection of books and articles from academic sources with a scientific foundation. A pitfall of this methodology was the significant amount of work needed to filter articles, which frequently involved sifting through multiple articles and trial and error in determining the appropriate key terms. Another issue was that when finding appropriate articles, the most useful ones were often unavailable.

Figure 1: Consort chart describing article selection process

Key search terms: drugs, opioid crisis, neurobiological mechanisms, impact, addiction, neurobiological and neurotransmitters.

Exclusion criteria: articles published prior to 2000, and written in the English language.



Chapter 3: Results

There are four categories for people who have tried an addictive drug, the first one being the ones who had an unpleasant experience and will never use it again. The second one is the ones who will use it occasionally and socially for enjoyment and can stop truly using it anytime, followed by the ones that use it often but nevertheless can give it up easily. Lastly, some use drugs regularly and frequently and find it impossible to stop using them, or at least only very difficult, and even then, they are likely to relapse (Goldstein, 2021). This last category of addicts represents the greatest challenge for society and neuroscience. The key distinction between these groups is the level of control they have over their drug use. The last group, the addicts, have lost control and are compulsively driven to continue using the drug despite negative consequences. That is because drug addiction is a complex neurobiological disorder that involves changes in brain function, making it extremely difficult for this group to give it up (Goldstein, 2021).

Neurobiology of Cravings

Drug addiction is characterized by a relapsing cycle of intoxication, bingeing, withdrawal, and craving. Unlike casual use or physical dependence, drug addiction reflects a persistent pattern of compulsive drug seeking and taking that persists despite diminished pleasure from the drug and severe negative consequences on the individual's well-being and quality of life. The focus of early addiction research has been on investigating the rewarding effects of drugs of abuse on the brain's dopaminergic system, particularly the limbic system. Drugs trigger a surge of dopamine release in the brain's reward pathways, leading to a pleasurable "high" that reinforces continued drug use (O'Brien et al., 2006). However, with chronic drug use, the brain undergoes neuroadaptations that reduce the sensitivity of the reward system and increase the activity of stress-related circuits. This leads to the negative emotional states and intense cravings

that drive the compulsive drug-seeking behavior seen in addiction, even as the user experiences diminished pleasure from the drug (Ceceli et al., 2022).

Substance Use Disorder is a complex neurobiological disorder that involves changes in brain function that drive compulsive cravings often followed by use, which leads to relapse even after a long period of abstinence, which poses a major obstacle to effective prevention and treatment. (Goldstein, 2021). A new diagnostic standard for Substance Use Disorders in the DSM-5, the most common, expensive, and fatal form of psychopathology, is craving, which is a strong desire for drugs. The roles that drug cues and cravings play in drug use and relapse remain disputed despite decades of research (Vafaie & Kober, 2022). "The majority of conditioned drug cues for humans are environmental in nature and include things like the sight of drug supplies and interoceptive cues like stress" (Vafaie & Kober, 2022). As clinical studies have repeatedly demonstrated, humans respond to drug-associated stimuli by releasing dopamine, conditioned sympathetic activation, and associated neural activity in areas such as the ventral striatum (Vafaie & Kober, 2022). While the degree of cue reactivity may predict drug use, some research indicates that cue exposure may cause people to seek drugs. As a result, drug use has long been conceptually associated with cravings, which is a complex psychological phenomenon. Drug cues and craving indicators are key mechanisms underlying substance use disorders and play significant roles in drug use and relapse outcomes (Vafaie & Kober, 2022). These findings provide clinical support for integrating craving assessment into treatment plans at every stage, even in primary care.

Neurobiology Of the Addicted Brain

Brain imaging research has revealed the complex neuronal circuits that mediate the relapsing pattern of addictive behavior. During intoxication, drugs of abuse trigger large bursts of

dopamine release in the brain's reward system, including the nucleus accumbens and dorsal striatum. This dopamine surge reinforces drug-taking behaviors and strengthens the conditioned associations between drug cues and the expectation of reward. Paradoxically, in individuals with addiction, the drug-induced dopamine response becomes attenuated, contributing to the reduced subjective experience of reward during intoxication (Volkow & Boyle, 2018)

As the intoxicating effects wear off, the addicted individual enters a withdrawal phase characterized by negative mood, increased stress reactivity, and significant dysphoria and anxiety. These aversive symptoms are mediated by brain regions like the extended amygdala and habenula, which show heightened activity during withdrawal. In parallel, the dopamine reward/motivation system becomes hypofunctional, further contributing to anhedonia and negative emotional state. Finally, during the craving stage, drug cues elicit dopamine release in the striatum, triggering the urgent motivation to seek and consume the drug. This craving response involves prefrontal, hippocampal, and amygdalar circuits that attribute salience to drug-related stimuli and mediate conditioned responses (Volkow et al., 2019)

While the mesencephalic and striatal regions have been the primary focus in describing the reward-related properties of drug addiction, the devastating effects of drugs on the prefrontal cortex (PFC) have been overlooked. The PFC is a crucial brain region that orchestrates higher-order executive functions, including reward-related decision-making, value tracking, goal-directed control, and inhibitory control (Goldstein & Volkow, 2002). Specific PFC subregions play distinct roles in addiction-related processes. The orbitofrontal cortex (OFC) regulates reward and punishment-related behaviors, potentially by representing the value of motivationally salient outcomes. The ventromedial PFC (vmPFC) is involved in making advantageous and goal-directed decisions, and its impairment can lead to the selection of

habitual behaviors despite unfavorable consequences. The ventrolateral PFC (vlPFC)/inferior frontal gyrus (IFG) regulates response selection and inhibition. The dorsolateral PFC (dlPFC) is involved in attention allocation, working memory, and emotional regulation. The anterior cingulate cortex (ACC) processes error monitoring, reward-based decisions, and emotion regulation (Ceceli et al., 2022).

Reward-related Decision-making/Choice and Insight into Illness

The maladaptive engagement of brain networks that mediate adaptive interaction with the environment may be a driving force in the debilitating cycle of disadvantageous behaviors and reward-related decision-making in drug addiction. Addicted individuals consistently exhibit risky decisions and impairments in maintaining optimal choices, as measured by tasks like the Iowa Gambling Task which is a psychological task used to assess decision-making under uncertainty and risk (Hultman et al., 2022). This is accompanied by alterations in the activity of brain regions like the anterior cingulate cortex, dorsolateral prefrontal cortex, inferior frontal gyrus, and striatum during reward-related decision-making. The blunting of prefrontal signaling during outcome anticipation or receipt may interfere with successful error monitoring and updating of decision strategies in addiction (Ceceli et al., 2022).

Preclinical studies have shown that chronic cocaine exposure can lead to increased perseverative errors and decreased exploratory rule-breaking in cognitive flexibility tasks, indicating impairments in the ability to shift to a new rule (Ceceli et al., 2022). Despite cocaine being an addictive substance, most people who use it recreationally for long periods of time do so without becoming dependent (Caded & Bisagno, 2015). Given cocaine's high prevalence in the general population, it is crucial to document any potential cognitive effects of the drug. According to recent neurobehavioral research, heavy cocaine users exhibit a variety of cognitive

impairments that may be related to modifications in brain morphology and function brought on by cocaine. The cognitive deficits from the neurobehavioral research conducted by Jean Lud Caded and Veronica Bisagno are the following:

- Impairments in executive function, decision-making, and increased impulsivity
- Abnormal Visual perception, psychomotor speed, and manual dexterity
- Deficits in verbal learning and memory functions
- Poor insight, judgment, and disinhibition

The hypofrontality that chronic cocaine users exhibit when completing attention and executive function tasks suggests that these cognitive alterations are probably linked to functional dysfunctions in the prefrontal cortex (Caded & Bisagno, 2015). However, even recreational cocaine users who are not dependent on the drug show mild cognitive deficits in all of these areas. Given the high rate of cocaine use for recreational purposes in the general population, this suggests that documenting the possible cognitive effects of cocaine is an important public health issue (Mahoney, 2019).

Importantly, a large proportion of individuals with persistent drug use disorders do not perceive a need for treatment, which may be partly attributed to neurocognitive impairments related to reward-related decision-making and impaired insight into the severity of their illness. Studies have found that addicted individuals show poor awareness of errors, discordance between actual and perceived choices, and impaired metacognitive accuracy, which are associated with dysfunctional activity and reduced volume in the rostral anterior cingulate cortex. These findings suggest that insight-oriented treatment strategies could be a promising avenue for tackling problematic drug use, especially in those exhibiting these awareness deficits (Ceceli et al., 2022).

Access to Treatments

Despite the effectiveness of substance use treatment, only a few people with a substance use disorder receive any type of specialty treatment. Current estimates show that only about 10% of Americans with a diagnosable substance use disorder receive treatment (Ignaszewski, 2021). There are significant disparities in who accesses addiction treatment. White men have the highest likelihood of receiving evidence-based treatment, while many vulnerable populations are less likely to be screened or treated for substance use disorders:

- Women with opioid use disorder are less likely to access treatment, be prescribed medications, and receive naloxone after overdose. Pregnant women face additional barriers due to fear of legal consequences and provider discrimination.
- Black patients may be less likely to receive treatment for opioid use disorder in primary care settings and have lower odds of completing treatment.
- In the correctional system, medication-based treatment for opioid use disorder is infrequent, leaving former inmates at a 13-fold increased risk of death in the first two weeks after release.
- Youth under 25 receive only about one-tenth of the treatment for opioid use disorder compared to adults, with nearly 70% receiving no treatment within 30 days of an opioid overdose.

These disparities in access to effective addiction treatment are particularly concerning given the well-established benefits of treatment, including reduced mortality, morbidity, crime, and improved general health and well-being. Addressing these systemic barriers to treatment access is crucial for improving outcomes for individuals and communities affected by substance use disorder (Ignaszewski, 2021)

Treatment for SUD

"Non-pharmacological interventions are those which do not involve a medication prescription and can be used in conjunction with other interventions, such as medication or alone" (Megranahan et al., 2023). According to a study conducted by Megranahan, Megranahan, & Cooper, there are three types of non-pharmacological interventions used to treat people who seek recovery through substance use treatment services. (A) information provision and dissemination, (B) non-specialized face-to-face contact, and (C) therapeutic interventions provided by a qualified person (Megranahan et al., 2023). In addition to these non-pharmacological methods, lived experience organizations, equine-assisted therapy, sports, purposeful activities, and creative arts interventions can also be useful methods of recovering from substance addiction. Megranahan and Lynskey conducted a systematic review of creative arts interventions and discovered evidence supporting the efficacy of music-based interventions in lowering cravings and boosting motivation for recovery. Research by Michael Silverman has established a strong indication of the benefits of using music therapy in substance use treatment centers. Silverman emphasizes the need for more quantitative exploration of music therapy interventions to enhance the limited body of evidence in this area. In summary, while the current evidence supports the use of music-based interventions for substance use disorders, particularly in reducing cravings and increasing motivation, more high-quality research is needed, especially on emerging non-medicalized recovery approaches like creative arts therapies (Bourdagh & Silverman, 2023).

Another way of treating SUDs is through a pharmacological approach. Pharmacological treatments have also demonstrated efficacy. For Example, nicotine replacement therapy can increase the chances of quitting smoking by 25-102%, while medications like bupropion and

varenicline can increase quit rates by 64% and 124%, respectively. Bupropion is a weak reuptake inhibitor of norepinephrine and dopamine, and also acts as an antagonist at nicotinic acetylcholine receptors (nAChRs). This may help improve cognitive processes like attention in smokers during nicotine withdrawal, though the effects on cravings have been mixed (Ashare & McKee, 2012). Animal studies show varenicline reduces nicotine self-administration and dopamine release in the brain. Varenicline has more consistently been shown to reduce cue-induced cravings in smokers compared to placebo, though the effects on brain activity have been inconsistent (Ashare & McKee, 2012). Combination treatment approaches are even more effective, nearly doubling quit rates (McGovern & Carroll, 2003).

For alcohol use disorder, research indicates that up to one-third of patients will abstain or substantially reduce their alcohol use in the year after a single treatment event, with an additional 10% using alcohol moderately. Treatments can include 12-step programs, cognitive-behavioral therapy, motivational interviewing, and pharmacological agents (Ignaszewski, 2021).

Medications for opioid use disorder, such as buprenorphine, have been shown to dramatically reduce the risk of overdose death, from 50-80%. Maintenance treatment with buprenorphine has been associated with 75% abstinence at one year, compared to 0% abstinence and 20% mortality when used only for detoxification (Ignaszewski, 2021).

For other drugs of abuse, where replacement agonist treatments are not available, psychosocial interventions like counseling, motivational interviewing, cognitive-behavioral therapy, and contingency management have demonstrated positive effects on reducing use. However, the treatment of substance use disorders is often siloed from mental health and other medical services, with only half of those with co-occurring substance use and psychiatric

disorders receiving appropriate integrated care. Improving access to comprehensive, integrated treatment remains an important goal (McGovern & Carroll, 2003).

Chapter 4: Discussion

Summary

By recognizing addiction as a chronic brain disorder influenced by various biopsychosocial factors, the research aims to dissect the intricate neurobiological mechanisms underlying addictive behaviors and neurotransmitter systems' involvement. This study delves into the multifaceted nature of substance use disorders (SUDs), particularly focusing on addiction to hard drugs such as cocaine, heroin, and opioids. To better understand the complexities of addiction, the study looks at how addictive behaviors affect neurocognitive processes like impulsivity, cognitive control, and decision-making.

Through a systematic review of secondary research, the discussion expanded to include disparities in access to addiction treatment, the effectiveness of non-pharmacological and pharmacological interventions, and the importance of integrated care for individuals with co-occurring substance use and psychiatric disorders. By adopting this multifaceted perspective, the research aims to provide a more holistic understanding of addiction and guide the development of more effective prevention and treatment strategies. The ultimate goal is to improve the lives of individuals and communities affected by the devastating consequences of substance use disorders.

Conclusions

Addiction is driven by changes in the brain's reward, stress, and executive function systems, and key neurobiological mechanisms include Increased incentive salience and compulsive habits in the basal ganglia during the binge/intoxication stage, decreased brain reward and increased stress responses in the extended amygdala during the withdrawal/negative affect stage compromised executive function in the prefrontal cortex, leading to impaired

decision-making and impulse control in the preoccupation/anticipation stage (United States Department of Health and Human Services, 2017). Drug addiction must be seen as a complex neurobiological disorder that requires multifaceted treatment approaches that address both the biological, psychological, and sociological aspects of addiction. This suggests a shift towards integrated care models that provide comprehensive support for individuals with substance use disorders, including access to both pharmacological and non-pharmacological interventions (Heilig et al., 2021).

There are well-documented disparities in the accessibility of addiction treatment, with some vulnerable groups—such as women, racial/ethnic minorities, and young people—facing major obstacles to getting the care they require. Several intricately intertwined systemic factors, such as structural racism, economic disadvantage, and a dearth of culturally sensitive services, are responsible for these disparities. For instance, research indicates that even after adjusting for variables like insurance status, Black and Latino people with drug use disorders are less likely than their White counterparts to receive specialized addiction treatment. To address these disparities, a comprehensive, integrated approach to addiction care is essential.

Integrating addiction treatment with mental health services, primary care, and social services can help address the complex, co-occurring needs of individuals with substance use disorders. Culturally adapted, evidence-based interventions that consider diverse populations' unique social and cultural contexts are particularly important. In addition to that, on-pharmacological interventions, such as information dissemination, face-to-face contact, and therapeutic interventions, have shown promising results in increasing the likelihood of quitting smoking and reducing cravings. Additionally, pharmacological treatments, including nicotine replacement therapy, bupropion, varenicline, and medications for opioid use disorder, have

demonstrated efficacy in reducing substance use and improving treatment outcomes. The findings emphasize the importance of offering diverse treatment modalities to meet patients' individual needs and enhance treatment effectiveness.

These conclusions have significant implications for policy, practice, and research in addiction treatment. Policies should prioritize addressing disparities in treatment access and promoting integrated care models to ensure equitable access to comprehensive treatment services. Practitioners should adopt a personalized approach to treatment, offering a range of evidence-based interventions tailored to individual needs. Further research is needed to advance our understanding of addiction neurobiology and evaluate the effectiveness of novel treatment modalities, particularly in addressing the complex interplay between neurobiological, psychological, and social factors in addiction.

Limitations

While reviewing studies regarding substance addiction, I came across some major limitations in addiction research. One of them was using self-report data, which is prone to response bias and underreporting. For instance, individuals may be reluctant to accurately self-report their use of illegal or stigmatized substances due to fear of negative consequences. Another limitation of addiction research is the administration of self-report measures. This method can miss a significant amount of recent drug use. Instead, more objective measures should be taken, such as urinalysis and hair analysis, for more accurate data. Sample size and data limitations, such as inconsistent reporting of prevalence rates and differing interpretations of assessment tools, can also harm the generalizability of research findings.

It will be essential to overcome these methodological, conceptual, and data-related constraints in order to further our understanding of addiction and create more potent preventative and treatment plans.

While this paper gives an overview of the basics of the science behind addiction, this is just a basic overview. There is still a wide array of information on this topic. With more than fifteen weeks to work on this project, the wealth of knowledge, along with all of the articles, could have been explored, such as addiction and special populations such as veterans, LGBTQ+, homeless people, etc. More time may have also allowed me to create a new study. This would have been a whole process of its own as the data collection could be an issue as drug addiction is a sensitive topic, and the IRB is not a quick system and could not have approved the topic. Other research platforms could have also been used, as many articles were not available through Anna Maria College's database platform.

Recommendations for Future Research

My original inspiration for this paper came from a short essay I wrote in a neuropsychology class, as I wanted to keep the topic going and expand more on treatments. I wanted to incorporate more work and evaluations on the topic, but I did not have the time. Another semester has been devoted to Drug addiction, and still, it feels unfinished. The study of Drug Addiction in the scientific direction can go in more ways than one. For instance, we have seen how people get addicted and how they recover. We might also dive into what it is like to go through recovery when a person suffers from mental disorders at the same time as the addiction. There are so many directions this work could take someone.

In the spirit of my literature review, an argument from the book *Broken*, a book about addiction and redemption, stood out to me, and it could also be a new way to take this topic. The

protagonist is having an interview with a person who works for an addiction recovery center (Hazelden). They are discussing how the federal government spends billions of dollars on the "war on drugs." Yet, most of the resources are spent on interdiction and punishment, and the "leftovers" are split between researchers who are studying the study of addiction, prevention programs for schools and communities to prevent people from using alcohol and drugs, and finally, treatment professionals who help addicted people into recovery and treatment (Moyers & Ketcham, 2007). To truly address the addiction crisis in America, policymakers must shift the focus and funding towards a public health-oriented model that provides accessible, high-quality treatment and sustained support for individuals and families affected by substance use disorders. Only then we can hope to help the millions of Americans struggling with addiction find lasting recovery and redemption.

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