What Are Possible Solutions to Addiction?: A Focus on Psychology and Biology

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Abstract

Within the past year, addiction has reached an all-time high with over 88,000 people dying from alcohol use disorder and over 100,000 people from substance abuse disorder. Yet only 10-13% of people with addiction-focused disorders receive treatment. Common present day treatments focus on psychological approaches, such as rehab and counseling. While these approaches are effective methods, supplemental treatment options are needed to keep up with the rapid increase of these issues. Increased knowledge of genetics could provide an alternative solution to the recent rise of these disorders. In this paper, I will discuss the possible solutions to alcohol and drug addiction through both psychological and biological (genomic) methodologies.

Introduction

Addiction is a chronic and relapsing mental disorder. The condition can lead to the deterioration of both mental and physical health for individuals (Brande, 2023). This includes mental issues like anxiety and depression, along with internal damage to organs, such as the kidneys and liver. The most common addiction is substance use disorder (SUD) which is characterized as a heterogeneous condition with the uncontrollable ability to use despite the harmful consequences (Mental Health Foundation, 2022). These substances are commonly used as coping mechanisms from personal matters, whether it be for stress, trauma, or other arduous feelings. As addiction develops, it changes the way the brain functions. Consuming drugs or alcohol triggers surges of dopamine and other “feel-good” neurotransmitters ten times the natural amount, overloading the brain’s receptors. Over time, the brain associates this rush with certain substances and builds a tolerance to the original levels of dopamine. Achieving this pleasure now requires more substances to gain the sensation you crave, creating a pattern of addiction (Yale Medicine, 2022). Long-term, heavy usage can permanently change the structure and functions of the brain (Mennis et al., 2016).

There is no one solid factor that determines whether a person will become addicted or not (NIDA, 2018). It is a combination of both nature and nurture. However, genetics do play a significant role, “influencing the numbers and types of receptors in people’s brains, how quickly their bodies metabolize drugs, and how well they respond to different medications” (NIDA, 2019). Every person receives one half of their genome from one parent and one half from their other. This means that parents who have SUD will contain specific variations in their genes that can be passed down to their offspring. Inherited levels of dopamine “can fuel poor impulse control and tilt someone toward addictive behaviors” (Cleveland Clinic, 2023). People that are closely related to others with addictions are at a predisposition to addiction themselves. Yet,

genetics are not the sole factor of addiction. A person's environment is also a large contributor. Being in surroundings with access to substances of abuse lowers barriers for acquiring, which aids the initiation for use. This can include a higher frequency of substance outlets, friends or family with substances, and social attitudes towards certain substances.

SUD represents a tremendous threat towards humanity, with "46.3 million people in America aged 12 or older meeting the applicable DSM-5 criteria for having a substance use disorder in 2021". Correlations have been observed between addictions and mental illnesses, with 13.5 percent of young adults aged 18 to 25 having both SUD and any mental illness in the past year. Despite noticeably effective treatments, in 2021, 94% of those affected by SUD aged 21 or older did not receive any treatment (SAMHSA, 2023). The statistics present a global issue and the numbers only continue to grow, making the need for a solution even more prominent. In this review, I will discuss the possible psychological and genomic approaches to tackle the problem.

Addiction is a complex phenomenon that results both from *and* in epigenetic modifications. Epigenetic modifications are alterations in gene expression due to one's environment (CDC, 2022). Epigenetic changes cause genes to be overexpressed ("turned on") or repressed ("turned off") depending on what chemical marks are present at a particular gene. While most epigenetic marks are reversible, they can have lifelong impacts (Harvard University Center on the Developing Child, 2010).

Epigenetics Introduction

In particular, early life experiences can have profound impacts on the epigenome, which is the accumulation of chemical marks on the genome. Life experiences, whether positive or negative, not only affect people's behaviors and health, but they can also cause changes in how their genes work. These epigenetic alterations can contribute to the persistence of addiction, as they can lead to long-lasting changes in the brain's structure and function. Specifically, epigenetic modifications can cause changes in cell plasticity, which is, in short, a cellular memory of environmental events, including learning and memory. This can thus lead to defects in neuronal communication, which may result in many of the characteristic manifestations seen in those with addiction (González-Pardo et al., 2013; Nestler et al., 2019). For example, if the brain's reward system is rewired through epigenetic changes, individuals with addiction have increased impulse control and stress responses. This results in a higher risk of relapse due to the brain retaining particular gene expression patterns. Even when an addictive substance or behavior is no longer present, epigenetic changes can persist, leading to the brain telling the body it "needs" more of a certain substance or behavior to experience pleasure or satisfy a craving.

In general, epigenetics can have huge implications on our understanding of psychology, particularly when examining gene-environment interactions. Studying what experiences, behaviors, or traumas result in epigenetic modifications can help inform us how psychological disorders are influenced by a combination of the environment and the genome. “Understanding the mechanisms involved in the initiation, maintenance, and heritability of epigenetic states is thus an important aspect of research in current biology, particularly in the study of learning and memory, emotion, and social behavior in humans” (Weaver, 2023). These genomic responses to environmental changes help form the basis for “phenotypic plasticity,” which informs the way people are able to cope with life changes, solve problems, and navigate the world. They serve as important factors when considering addiction and how best to treat patients.

Psychological Approaches

Addiction has been an ageless issue, dating back centuries throughout the world and to this day continues to be a global matter (American Addiction Centers Editorial Staff, 2023). The earliest form and most traditional treatment has been behavioral and counseling treatments. This approach consists of different types of therapies including, cognitive behavior therapy (CBT), contingency management, family therapy, group therapy, and motivational interviewing. A common type, CBT, aims to teach people to find the connections between their thoughts, feelings, and actions to increase their awareness of the impact these things have on their recovery. When a person is able to understand why they feel a certain way and how those emotions lead to substance usage, they have a better chance of overcoming their addiction. Certain feelings after a negative situation can cause a cycle of pessimistic thinking, leading to substance usage as a coping mechanism. What CBT does is stop these negative patterns by breaking down the why behind a person’s reaction through goal-oriented therapy sessions. The therapist focuses on analyzing a person’s behaviors and thoughts, then suggesting changes the person can make in their life through a gradual process (NHS, 2022). The treatment has been proven to have an effect on substance abuse, having numerous studies and research supporting its effectiveness (Magill & Ray, 2009; David et al., 2018). Within CBT alone there is a variety of specific versions that address certain issues. Dialectical behavior therapy (DBT) is a type of CBT that is efficient with people suffering from SUD. While CBT focuses more on how people’s thoughts, feelings, and behaviors interact with each other, DBT places an emphasis on regulating and processing emotions along with embracing modified behaviors. This therapy uses techniques, such as mindfulness, distress tolerance, and emotion regulation, to help the patient understand and function with their emotions. Another type of CBT is rational emotive behavioral therapy (REBT). Unlike CBT, REBT emphasizes a focus on the underlying causes and core troubles rather than modifying the behavior itself. This type uses confrontative methods such as reframing and de-catastrophizing with the aim of challenging irrational thought processes.

A different method, contingency management, is a treatment used where individuals are “reinforced” or rewarded for positive change in behavior. This technique is based on operant conditioning principles, the method of modifying behavior through reinforcement or punishment. It has been used in everyday settings such as pet training or employment incentives, as well in clinical settings like treating individuals with SUD (Petry et al., 2011; Pfund et al., 2021). The aim of this treatment is to encourage individuals to continue using positive mindsets by an external motivation. Once a behavior is rewarded, the behavior is now reinforced and its frequency of occurrence increases. For people suffering from SUD, the treatment can be shown when receiving a reward for reaching a sobriety goal. Individuals are now more likely to continue this sober behavior when an incentive is included.

An alternative practice, family counseling, is based on the systems theory, which is the concept that an individual is a part of several systems - family, community, culture, and society. Addiction is a disease that spreads in a family, not just an individual. Family members can unknowingly enable hurtful behaviors while individuals with the disorder can damage their relationships through self harm (SAMHSA, 2020). The disorder is often linked to other complex issues within a person’s life. Family counseling focuses less on the individual's thoughts and behaviors and concentrates more on the individual’s relationships with family, friends, and environment, analyzing how SUD is embedded in the interactions within a family. This treatment gives both the individuals with a disorder and their family members a safe place to express difficult emotions by using a non-blaming, collaborative approach. Familial support encourages the addicted individual to pursue sobriety with a positive mindset, for both themselves and their family.

Similar to family therapy, group therapy uses the support of others to encourage sobriety. However, this therapy consists of people that suffer from the same disorder. Examples include informal groups, such as alcoholic anonymous programs to more structured groups like recovery retreats, where people of the same issue gather together to share in an open space. These groups create a positive peer support system, allowing deep rooted connections to be formed from relatable experiences and emotions. The therapy reduces the sense of isolation many addicted individuals feel and shares different ways people process their similar issues. Being in a group allows people to witness the success of their peers, which gives hope to others (SAMHSA, 2005). Group therapy has proven its success endless times, shown through the thousands of stories from recovered individuals who participated in these programs.

A more personal one-on-one approach is motivational interviewing, which is a person-centered approach between client and provider. This treatment interweaves four methods: partnership, acceptance, compassion, and evocation. Having a provider be empathetic and intent to understand the client’s perspective which creates a space the client feels comfortable to share in. Using compassion and evocation to prioritize the individual's needs and identify the

motivation within the person, they feel empowered to overcome their disorder and reach sobriety through an independent process. The sessions between the client and provider are labeled as interviews, shaping the situation to seem like a collaboration rather than a confrontation. The focus of this therapy is to invoke the individual's own motivation. When the individual feels responsible for their own actions and achievements, they are more likely to stay sober, proving itself as a useful treatment (Hoeg, 2023).

Genetic Approaches

For years now, these various therapies have assisted people towards sobriety through numerous psychological-rooted methods. However, the treatments alone are not enough since “94% of people aged 12 or older with substance abuse disorder did not receive any treatment” and “nearly all people with substance use disorder who did not get treatment at a speciality facility did not think they needed treatment” (SAMHSA, 2023). Despite the evidence from these therapies, people choose to not receive treatment, and out of those who do, “85% of individuals relapse and return to drug use within 1 year of treatment” (Brandon et al., 2007). Substance users aren’t ready to stop using, partially because they are scared of the unknown outcomes that follow. Though psychological approaches are effective, the success of treatment varies from person to person and depends on several different individual factors. People need reassurance, the comfort of knowing that a treatment will work and that the effort used to achieve sobriety is worth it. Biological-focused treatments in the fields of genetics and cellular biology provide that solace through precise methods and evidence.

While the phenotypic outcomes of addiction have been well-documented, the genetic underpinnings of addiction are still not fully understood. To gather more insights into the genetic and molecular drivers of addiction, technologies such as Genome-Wide Association Studies (GWAS) and whole genome and whole exome sequencing can help identify genetic variations, called single nucleotide polymorphisms (SNPs), in those with addiction. Identifying common SNPs may help researchers better understand the genetic differences that cause individuals to become more susceptible to addiction (NIDA, 2019). One example of using sequencing analyses to identify a genetic driver of addiction was in the recent discovery linking CHRNA2 to cannabis use disorder. Researchers performed a GWAS that identified a “significant risk locus on chromosome 8” that controls the levels of the gene *CHRNA2* expressed in the brain (Demontis et al., 2019). *CHRNA2* encodes for the α2 subunit of neuronal acetylcholine receptors, which are important for the binding of neurotransmitters. Scientists found that neuronal acetylcholine receptors modulate the withdrawal of THC, which is the main active ingredient in cannabis (Buzzi et al., 2023), thus playing a major role in cannabis use disorder susceptibility. Specifically, low levels of this α2 subunit, CHRNA2, in the cerebellum is associated with increased risk for cannabis use disorder. This discovery offers a potential therapeutic approach for cannabis use disorder: selectively target the α2 subunit of neuronal

acetylcholine receptors. This provides a proof-of-principle study that genomic analyses could provide potential targets for future prevention strategies, therapies, and medications.

Utilizing genomic data to uncover SUD targets is a promising approach for developing new therapeutics. Once a target is identified, though, how do scientists actually develop treatment options? Gene therapies might be the answer. Gene therapy aims to modify or manipulate genes with the goal of treating or curing a disease (U.S. Food & Drug Administration, 2018). In specific, gene editing technologies are pioneering new methods of substance use treatment. Gene editing would allow scientists to fix mutations or alter gene expression in cells *ex vivo* then implant or transfuse these “corrected” cells back into patients. In a mouse study, scientists performed gene therapy that helped mice overcome cocaine addiction (Li et al., 2019). They used a relatively novel gene editing technology, called CRISPR/Cas9, to edit skin epidermal stem cells so that they express an enhanced form of butyrylcholinesterase, which is an enzyme that breaks down cocaine. These edited skin cells were then transplanted back into the mice, leading to long-term release of the enzyme. This method of treatment led to decreased addiction to cocaine, as well a drastically higher ability to protect against overdose, in comparison to untreated control animals. Therefore, skin gene therapy and transplantation may serve as a fruitful method for drug elimination and overcoming addiction in human patients.

In a separate study, again using CRISPR/Cas9 gene editing technology, scientists were able to treat binge alcohol exposure in rats. Previous research has shown that adolescent alcohol exposure in rats results in epigenetic modifications to a gene responsible for synapse activity in the amygdala of the brain (Kyzar et al., 2019). These epigenetic modifications result in increased anxiety and alcohol consumption in adulthood. By identifying epigenetic changes that cause increased susceptibility to SUDs, scientists can use these as therapeutic targets. In this instance, scientists were able to use CRISPR gene editing to reverse the epigenetic changes. This caused the gene to return to normal expression levels and resulted in a significant reduction in anxiety and alcohol consumption (Bohnsack et al., 2022). Therefore, gene editing and gene therapy show potential for incorporating various genetic information to prevent or enhance treatment options for SUD.

Although promising, gene editing to treat addiction may raise ethical concerns and unintended consequences, potentially altering complex genetic pathways and behaviors in ways that are not fully understood or controllable. As an alternative, pharmacogenetic treatments have emerged as a promising avenue for treating SUD, offering personalized and targeted genetics-based interventions for individuals grappling with addiction. Every individual has a different genetic makeup, which can make treatment difficult. Pharmacogenetics offers an approach that tailors drug therapies based on a person’s DNA. By delving into the specific genetic variations that influence drug metabolism and response, healthcare providers can optimize medication

regimens, ensuring a more precise and effective treatment approach for patients with SUD (Haile et al., 2009). This personalized approach not only enhances the overall efficacy of interventions but also minimizes adverse effects and the risk of relapse, ultimately improving the quality of life for individuals combating addiction. Through the insights learned from pharmacogenetic research, the medical community is poised to revolutionize SUD treatment strategies, opening up a new era where genetic information plays a pivotal role in guiding therapeutic decisions and offering newfound hope for those affected by this challenging condition.

Conclusion

While SUD is an acknowledged problem, communities are failing to confront the issue with the urgency it deserves. The need for a change is clear: to combat the rise of addiction a combination of psychological and biological approaches are needed. The disorder affects the mind and body, therefore requiring treatment for both. Although this change would require large amounts of funding and time for research, from a long-term perspective, it would be a significant stepping stone for the upcoming generations. Transitioning to a focus on genetics while continuing psychological practices can make a sustainable impact on current methods, giving those who suffer a variety of alternative options.

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