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Genetics, Inheritability Factors and Addiction

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Abstract

Addiction along with drug use disorders requires exposure to addictive agents. The renowned addictive agents include drugs such as alcohol, nicotine, and other hard drugs. Individuals who are susceptible to addiction include those who are increasingly exposed to the addictive agents. Nicotine use and abuse of alcohol are the most abused substances in the globe. These substances are responsible for the increasing mortality in both developing and developed worlds. The risk factors for addiction range from genetic factors to environmental factors. Alcohol dependence is mostly attributed to the short (S) allele. Similarly, this dependence is also linked to the environmental factors. Like alcohol, nicotine dependence is also linked to genetic factors. Various genetic studies indicate that nicotine dependence is heritable as there are many genes responsible for inheritance of smoking behavior. This study however notes that addiction to drugs is as a result of either heritable or inheritable factors. The study used 2000 smokers, 3000 alcohol addicts and 3000 cannabis dependents as the population for research. The researchers evaluated the contributions of genes to substance dependence. The results of the study showed that genetic and environmental factors contributed significantly to the addiction disorder.

Keywords: Addiction; Dependence; Environmental factors; Etiology; Hereditary; Markers

Introduction

Disorders related to the addiction to drugs and substances are regarded as one of the major causes of deaths that, however, can be prevented by Slutske et al. But various genetic and environmental factors may greatly aggravate such a dependency, especially if take into consideration that most of them can be inherited. This fact was confirmed by the findings of the studies conducted on twins i.e., twin studies, according to which the addiction may occur due to the existence of genetic etiology. While examining the dangers of drug and substance abuse, it is crucial to comprehend the biological occurrences that cause addiction and establish drugs that can disrupt with cellular mechanisms to prevent and cure the dependence [1,2]. That is, the understanding of the factors that influence nicotine dependence is critical in lowering the rate of smoking [2].

Many researchers in the genetics of drug dependence indicate that addiction along with co-morbid psychiatric disorders present similar neurological features [3]. Similarly, many individuals have genetic parameters termed as polymorphisms that increase the risk of substance use addiction. According to Zhang et al. these genetic forms may become a threat, especially in association with various environmental factors including culture and availability of drugs since they expose an individual to drug abuse resulting in addiction [4]. Many studies have focused on alcohol dependence; however, hereditary influence of tobacco, cannabis, opioids and other substances have not been previously shown [5].

Study Objectives

This study is aimed at grouping and identifying addictions, evaluating the function of heritable differences of addictions and the intersection of hereditary impacts of alcohol and substance abuse. The study has employed various approaches in particular interviews and phenotyping techniques involving neuroimaging and endophenotypes results.

There are two dominant techniques applied to detect genetic factors that lead people to drug abuse and consequently to addiction [6]. One of them is a candidate gene method that takes into consideration hereditary factors which may determine vulnerability to addiction [7]. The candidate gene examination consists of dividing the deoxyribonucleic acid into various patterns of nucleotide known as gene markers. Investigation of these markers is carried out to analyze whether there is a relationship between the genes of an individual and the markers passed on together with the disorder in the families [6]. The other method is called genome-wide association linkage technique, in which all the genome is reviewed to identify the portions of integration among the phenotypes of the addicted individuals. Addictions are mainly recognized by the application of the Diagnostic and Statistical Manual of Mental Diseases, whereby substance dependence and abuse are placed in specific classes though the two terms may be used as one term called disorder [8].

Majority of the world population consume tobacco, alcohol in addition to other drugs. However, cigarette smoking is the most common since is the leading cause of mortality in the world. Approximately 400,000 persons die in the US from illness associated with tobacco [9]. With the increasing use of tobacco, it is expected that the death toll will increase to over eight million people annually in developing countries. Some studies also indicate that 13% of the persons in the US develop what is referred to as alcohol dependence later in life [9]. Addiction to these substances is attributed to either inheritable factors or heritable factors. According to Bierut the development of addiction is often triggered by initiation of drug use which finally results in the development of addiction as demonstrated in Figure 1. Use of nicotine is linked by many studies to heritability

factors. For instance, indicates that approximately 50% of nicotine dependence is as a result of heritability [9]. However, significant differences in nicotine addiction and disparities in dependence to alcohol can be attributed to inheritable factors and heritable factors respectively. The genes influence over forty percent of the individuals who are dependent on cannabis.

Likewise, two significant factors have been discovered to result in differences in heritability of drug and substance addiction. The first one deals with the levels of addiction. Addiction is a process that starts with initial levels of use succeeded by the escalation to frequent and prolonged utilization that can become difficult to control and may result in dependence [10]. The initial levels are not easily transmitted and are profoundly affected by the environmental factors [8]. According to Aghaii et al. environmental factors such as drug addiction of one of the family members, parental unemployment, and family conflict exposes individuals to initial stages of substance use (Figure 1). Similarly, they indicate that social factors like school, peers, unhealthy entertainment, and cultural poverty in addition to inadequate social acceptance influence some people to start using drugs [8]. On the same note, Carlier et al. indicate that genetic factors profoundly influence the subsequent stages addiction (Figure 1).

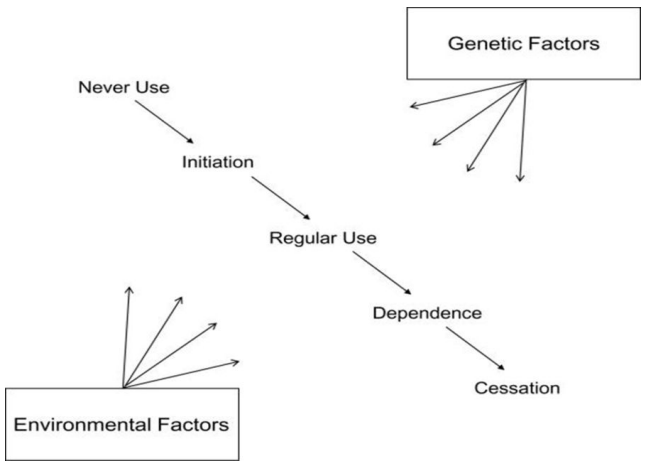

Figure 1: Indicate that genetic factors profoundly influence the subsequent stages addiction [21].

The other significant factor for variation of heritability of drug from substance addiction is the developmental process. Dependence follows a natural course hence, researching the function of the developmental course of addiction is difficult. The beginning of drug and substance abuse often takes place during adolescence while the dependence appears during the initial stages of adulthood [11]. Early adolescent drug abuse dramatically augments the susceptibility of lifelong substance use disorder since this stage allows the growth of risk-taking behaviors that is critical for survival [11]. According to Jordan and Andersen, early abuse of drugs impairs with the neurodevelopment which triggers neurobiological changes that increases the risk of SUD (Figure 2). Thus, there are significant differences in etiology on the grounds of whether it is an adolescent or a child who is under investigation. For instance, in many past accounts of alcoholism, heritability reduces immensely during the onset of adulthood.

Based on many studies, for the determination of the amount and frequency of utility and the number of abused, genetic factors possess a stronger effect in adults [12]. For drug abuse, there have been persistent facts that genetic factors may significantly affect the individual even at puberty.

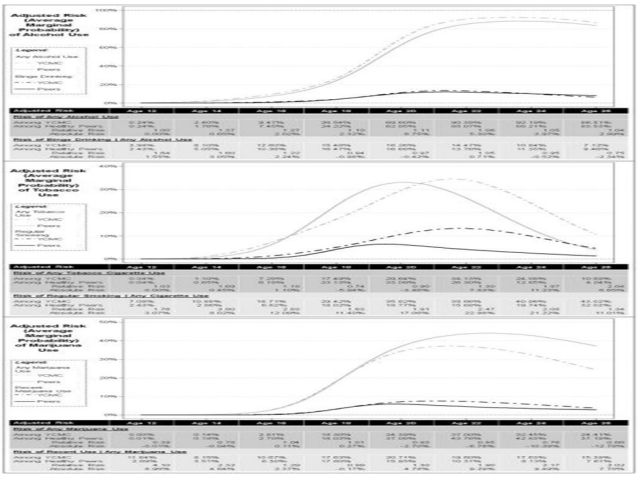

Figure 2: Demonstrates the increasing risk of using alcohol, tobacco, and other drugs by age. From the graphs, it is apparent that use of drugs increases with the users' age. Thus, drug dependence increases as adolescents advance in age [22].

Methodology

This study was based on face-to-face interviews findings as well as interviews conducted via phone to minimize movements to both the interviewer and the interviewee. The subjects involved included individuals addicted to drugs and substance, health and social workers dealing with the addicted people, and the relatives of the addicted individuals.

The interview involved the vast number of participants including around two thousand smokers, three thousand alcohol addicts, and three thousand cannabis addicts. One hundred and fifty-six health workers concerned with the welfare of the addiction victims were involved in the study as well. One hundred and thirty-four social workers participated. Four thousand relatives of the addicted victims were interviewed and laboratory-based assessments were also conducted.

Results

From the information gathered during the interviews, genetic and environmental factors are the primary influencers of the complex disorder called addiction. Some interviewees reported that addiction was caused by moral decline in the society. The availability of drugs at relatively cheap prices greatly facilitated the addiction (Figure 3). The data collected also revealed the significance of genetic factors and led to the finding of an inherited connection to the addiction. Furthermore, it was revealed that addiction is complicated, lacks homogeneity, and does not possess a distinct Mendelian fashion in its inheritance. Hence, recognizing the particular hereditary factors that cause addiction was difficult. The information collected also shows the function of genetic factors and environmental influences and their role in causing susceptibility to addiction. Addiction involves alcohol use disorders, dependence on nicotine, cannabis sativa, and cocaine. These

disorders are among the prevalent psychiatric conditions that were reported to cause the preventable deaths.

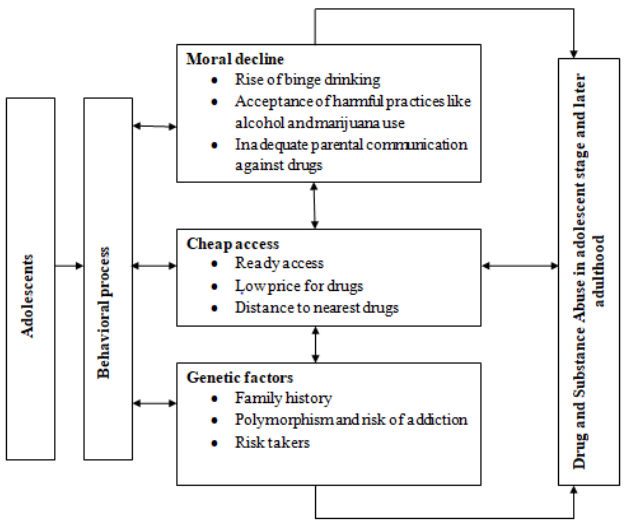

Figure 3: Summary of the participants' responses. **Note:** The above figure summarizes some of the factors that influence individuals to become addicted to drugs. The respondents of the study indicated that moral decline, availability of drugs, and genetic factors were the leading cause of drug dependence. They noted that rise in binge drinking, embracement of harmful practices in addition to inadequate parental involvement in guiding young people contribute significantly to rise of drug use in the society. Similarly, the respondents indicated that the increased availability of drugs as a result of cheap price and accessible market encourage many people to start as well as advance their use of drugs. Likewise, the respondents of the study indicated that dependence to drugs is also triggered by genetic factors. They noted that some people use drugs because it is a familial practice. Others claimed polymorphism in addition to risk taking habit exposed many people to drug addiction.

Drug-particular genetic factors

Alcohol dependence in addition to dependence on other substances usually co-occurs, and there is strong evidence that attribute these disorders to genetic factors. Indeed, studies indicate that the intersection in inheritable factors on alcohol, nicotine, and illegal drug is as a result of shared genetic factors [13]. For instance, twin studies show that genes influence the advancement of alcohol dependence as heritability estimates for both men and women is very high [13]. Based on Ducci and Goldman's claim, one can conclude that there is a strong correlation between alcohol dependence and drug dependence in monozygotic twins when compared with dizygotic twins. That is, heritability influences initiation of alcohol and other drug use [13].

Nevertheless, for nicotine addiction, hereditary influencers shared with alcohol and illegal substances are accountable for around thirty percent of inheritable differences. This means that there is a significant level of genetic uniqueness in individuals that use substances. In fact, Hu et al indicate in their study that self-medication also influences some people to use drugs [14]. In reference to this, they argued that individuals that suffer from schizophrenia often use tobacco to alleviate some psychiatric symptoms. Similarly, Hu et al. claim that use of nicotine lowers the side effects of the used anti-psychotic drugs. Based on this, it is apparent that inheritable factors also contribute to addiction to drugs. Concerning their pharmacology, multiple factors were reported to be responsible for the lack of gene uniqueness among the prohibited drugs. The increased level of comorbidity found in many addictions elevated the genetic intersection and declined the strength needed to determine substance-particular genetic factors. Several inheritable variants of moderate influence size affect this inheritable structure.

There exist two polymorphisms that are recognized for controlling alcohol metabolism, and according to the information collected, they have been found to contain a protective factor on the usage of alcohol. According to Crous-Bou et al. the polymorphisms of ADH1B and ALDH2, which are genes that predetermine the primary enzymes involved in alcohol metabolism, usually cause variations in not only the quantity of production but also oxidation of acetaldehyde in different people. Despite indicating this, Crous-Bou et al. learned from their study that there is little association between the two polymorphisms with the consumption of alcohol [15].

According to their results, polymorphism in ADH1B has insignificant effect on alcohol consumption. Similarly, polymorphism in ALDH2 has no association with alcohol consumption [15]. Contrary to Crous-Bou et al.'s finding, the serotonergic variants have also been included in the etiology of alcohol addiction. Nevertheless, a meta-examination of conventional researched serotonin transporter gene polymorphism discovered a feeble connection with alcohol dependence ($p<0.05$). In support of this finding, McHugh et al. indicate that there is a strong association between s allele with alcohol dependence [16]. Their findings showed that there is 15% likelihood of alcohol dependent individuals having more than 1 s allele [16]. In support of this finding, Tartter and Ray note in their study that polymorphism in 5-HTTLPR of the described serotonin transporter gene plays a critical role in the genetics of alcoholism. The polymorphism of this promoter region often results in two specific alleles, the L and S alleles. Although the S allele causes small effect, it influences the development of alcohol use disorders (AUDs) [17]. In addition to these findings, inconsistent relationships between diverse forms of cannabinoid receptor 1 hereditary factor were also reported.

Cannabinoids purportedly connect to the cannabinoid receptor 1 gene and the fatty acid amide hydrolase hereditary factor [18]. Helfand et al. further indicates that the two increases prevalence of addiction in humans as they are capable of deregulating reward-driven processes. Similarly, multiple genes were linked to diversified aspects of dependence on cocaine. They comprise dopaminergic single gene variants and dopamine beta-hydroxylase [7]. The nucleotides discovered to be connected with cocaine addiction in two free types of research contradictory. The diverse allelic forms of this gene marker that bring danger for addiction to nicotine portray abilities to offer protection from addiction to cocaine [7]. That is, ANK1 A1 as well as A2 allele can influence smoking cessation. Additionally, opioids link with the nucleotide encoding receptor mu-opioid to establish analgesic and relaxing impacts. OPRM1 gene is the most studied candidate gene which causes dependence on opioids and heroin [5].

The responses showed that the significant part of hereditary factors affects several drugs that cause addiction. Essential segments of innate impact on addiction to diversified substances can be accounted for similar genetic susceptibility. Dependence on nicotine and alcohol

consumption intersect with shared hereditary impacts. These linked genetic routes probably represent several processes. Addiction is attributed to the sequences of impulsivity and pressure. Various genes found in the dopamine reward cycles have significantly been researched in this regard [5]. The reward cycles contribute autonomously and jointly with glutamatergic and GABA-ergic signaling in the prolonged abuse of drugs and establishing and sustaining the addiction [5].

The reports showed that there are adjustments of the central nervous system in the reward cycles associated with impulsivity, addiction, and molecular processes of the activity of hereditary factors variants in these channels attributed to a particular drug addiction. The addicted subjects showed less awareness concerning the biological bases of dependence.

The reports revealed that the daily use of cigarettes recognized as 1051830 have a significant correlation with a polymorphism that has a functional non-sense gene in the nicotinic acetylcholine receptor group of genes.

Discussion

The initial primary field of development for this study was the chronological change from diagnostic grouping of impacted versus unaffected to a dimensional realization, for instance, statistics of quantity of drugs used per day, signs counts, factor counts derived from diverse indices of drug use, and other few variables showing susceptibility to addiction. Continuous measures of this kind are genetically transmitted, and this transmission intercepts significantly with genetic effects on addiction [19]. Furthermore, the continuous phenotypes have an advantage since heterogeneity does not bind them, for instance, giving a similar unaffected value to the subjects who do not drink alcohol, those who are modest alcohol takers, and those who are addicted. Therefore, certain people are usually at risk of abusing alcohol and other substances excessively because of genetic make-up and environmental factors [19].

Expectedly, addiction is examined through self-narration interviews, questionnaires, and clinical interrogations. Nevertheless, experiments in the laboratory were also applied to offer the analysis of individual variations in addiction using challenge conceptual frameworks in which extreme amounts of a drug are given to the subjects in a controlled environment. By using this concept, the study designed the stage of feedback phenotype for oral alcohol tests whose results were both positive and negative including nausea and different physiological and biomarker adjustments that were applied to recognize a reduced level of response of people who are exposed to high threats of alcoholism.

Endophenotypes

Endophenotypes were taken to mean the measurable indices of susceptibility to a phenotype. These parameters can be passed on to offspring and are proposed to be highly proximal to the natural supports of the habit being investigated. Despite their co-separation with the disorder, they are immensely closely associated with causes of the disease. Different putative endophenotypes exist and have been proposed for addiction to alcohol and substance, and they were regularly examined using an adjusted version of the common Stroop action and electro-encephalogram task. Many of these endophenotypes have been applied in the candidate gene examination, for instance, single nucleotide variants in GABRA2 have been discovered to relate with beta waves of resting electro-encephalogram [20].

Neuroimaging phenotypes

Even though the sample size was average, mainly because of prices and challenge of imaging technology, this method has started to record reliable results. The findings showed that some alcoholic families were also related to self-reported impulsivity and insula-cortex induction in females during expectation of rewards in the form of money. Insula-cortex is influenced by cue-activated drug desire and addiction and hence the researches have been showing the prospective neurobiological view on the connection between GABRA2 and dependence on alcohol [20].

Conclusion

In conclusion, addictions are critical conditions associated with disorders that may be repercussions or prospective causes of dependence. It is profoundly influenced by genetic and environmental factors. Majority of the alcohol dependents have at least 1 S allele that increases their risk to addiction. Similarly, serotonin transporter polymorphism also influenced alcohol dependence. Use of alcohol was however promoted by diverse environmental factors. Likewise, there is a strong association between nicotine dependence and genetics. The use of this drug is heritable as it is evident in majority of the users' genetic polymorphisms. However, other factors other than genetic factors influence use of nicotine in some individuals. Despite this, gene variants in brain dopamine demonstrate the effectiveness of pharmacotherapies in enhancing smoking cessation. The way we evaluated dependence is substantially associated with the impact of hereditary factors and genetic routes that are diagnosed. Use of several inter-linked strategies for the assessment of addiction in relation to genetic factors and determining their correlations with each other provides pathways for associating hereditary factors and habits.

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