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Review Article

The Role of Genetics in Human Addiction

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Abstract

Addiction (addiction) is a condition in which a person naturally suffers from a weakness of the will to control the repetition of his actions due to psychological reasons or the use of chemical substances, although the weakness of the will is not a disease, but due to the complications that have occurred on the person's central nervous system, it is assumed as a disease. and this disease causes the repetition of that behavior by disrupting control over the behavior-reward system. The disease of addiction disrupts the neural circuits related to the reward, motivation, and memory systems in the brain, and the disruption of these systems in the brain causes biological, physiological, social, and mental complications. Investigation of addiction as a psychological, social, and economic complication is done from the perspective of medical sciences, psychology, and sociology as well as from the perspectives of philosophy, law, ethics and religion.

Keywords: Addiction, Genetic factors, Psychology, Personality, Ecology

Introduction

Addiction (addiction) is a condition in which a person naturally suffers from a weakness of the will to control the repetition of his actions due to psychological reasons or the use of chemical substances, although the weakness of the will is not a disease in itself, but due to the complications that have occurred on the person's central nervous system, it is assumed as a disease and this disease causes the repetition of that behavior by disrupting control over the behavior-reward system. The disease of addiction disrupts the neural circuits related to the reward, motivation, and memory systems in the brain, and the disruption of these systems in the brain causes biological, physiological, social, and mental complications. Investigation of addiction as a psychological, social, and economic complication is done from the perspective of medical sciences, psychology, and sociology as well as from the perspectives of philosophy, law, ethics, and religion. Since 1964, the World Health Organization has recommended the use of the term drug dependence or drug dependence instead of the term addiction. In general, from a conceptual point of view, the disease of addiction is a main, chronic, and neurological disease, which develops and develops because of genetic, physiological, and social factors, so that the characteristic feature of this disease is a disorder in the control of performing actions, or a feeling of compulsion to perform A certain act, despite the knowledge of its dangerous consequences [1].

Addiction to drugs (drugs and alcohol), or abnormal habits, is a psychiatric and psychological disorder that, on the one hand, destroys the meaning of the word happiness in the life of a person and his family, and on the other hand, causes countless social and economic harms. it has. In another definition of drug addiction, it is chronic replacement addiction, that is, external drugs, whether herbal or chemical, and even alcohol, have replaced drugs or natural opioid-like substances in the human body or an addicted person. Of course, abnormal habits and behavioral addictions independent of chemical substances were not considered as addictions in official classifications until recent years, and it has been a short time since addictions such as Internet addiction, work addiction, and computer game addiction have been classified as a form of addiction. are paid attention to. One of the biggest problems of most countries

in today's era is the phenomenon of drug abuse, which directly and indirectly, short-term, and long-term, has overshadowed the quality of life of its residents [1,2].

Addiction is the body's physiological response to repeated use of addictive substances. On the one hand, this dependence causes temporary relief and relaxation and sometimes transitory stimulation and excitement for the person, and on the other hand, after these effects are over, it causes the person to search for the substance again and continue to depend on it. In this case, the person becomes dependent on the drug, both physically and psychologically, and must gradually increase the amount of the substance consumed [1,2].

Types of Addiction: Physical and Mental

Physical Addiction

It is the body's physiological response to the entry and effect of new substances into the body, which usually occurs with the phenomenon of tolerance (tolerance), which means that due to the increase in the number of nerve receptors and the decrease of nerve mediators in the central nervous system, the user's need increases every day. Withdrawal of physical addiction is associated with pain, insomnia, hypersomnia, and hangover. The duration of withdrawal from physical addiction is much shorter than mental addiction [1,3].

Psychological Addiction

It is caused by the pleasure and euphoria of drug use. It is precisely because of disrupting the order of the release of nervous mediators that a person suffers mental injuries or contradictions. For example, the drug methamphetamine (glass drug) increases the release of dopamine in the brain and causes a state of excitement, euphoria, concentration, etc. Now, after stopping the use, the person becomes drowsy, depressed, unfocused, etc., due to the decrease in dopamine levels. The length of the return period of these nerve mediators to the normal state is much longer and some even believe that they do not return. As a result, psychological addiction is much more deadly. Psychiatric addiction causes many ex-users to slip even after periods of several years. But unfortunately, people who seek profit to advertise drugs claim that they are not addictive, but in fact, all drugs are psychologically addictive, but some are not physically addictive [1,3] (Figure 1).

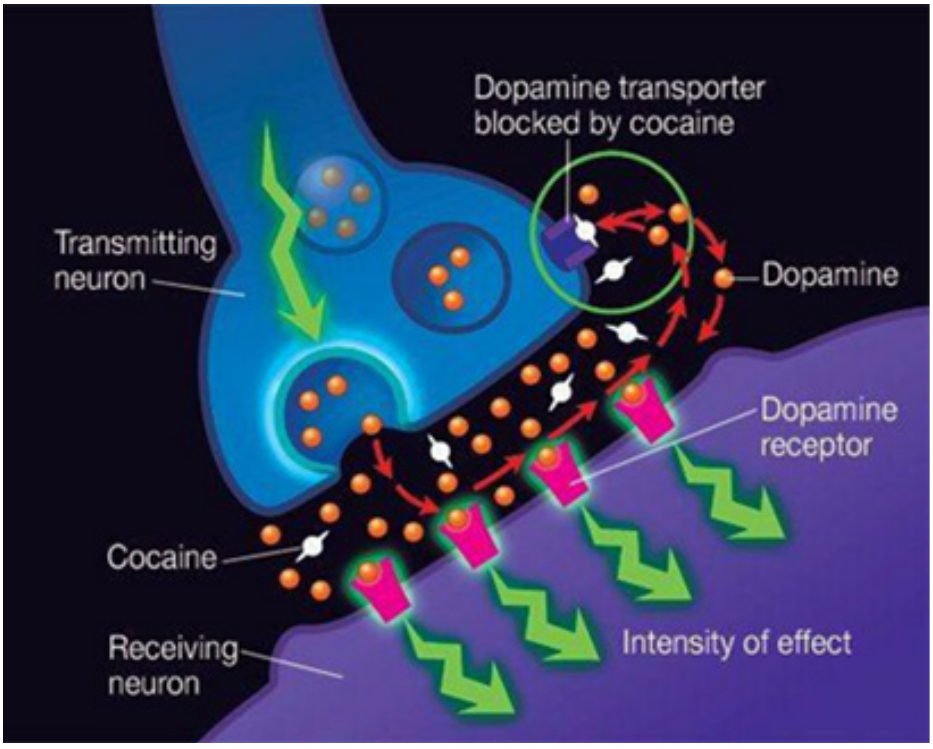

Figure 1: Schematic of the effect of cocaine on dopamine receptors [1].

Legal and Illegal Addiction

Addiction can be divided into two groups, legal and illegal. Legal addiction includes the continuous use of substances known as drugs. These medicinal substances may be natural or synthetic and may be taken by doctor's prescription or self-administered. Addiction to substances such as tobacco and cigarettes, which creates psychological dependence and causes continued use, is classified in the category of permitted addiction [1,4].

Illicit Addiction

A person's dependence on regular drug use in such a way that national or international laws recognize it as illegal is called illegal addiction [1,4].

Addiction can be considered as a chronic poisoning that is harmful to the person as well as to his family and society. Its types are as follows:

Opium: Which was mostly used among old people in the past, but nowadays it is distributed and consumed among young people and teenagers. Its consumption gradually increases the demand, and the person comes to a moment when he is unable to leave it [1,4].

Morphine: Which is obtained from opium and is consumed in both liquid and powder forms, the consumption of this substance is high among young people, and it is a sleeping substance and has the effects of opium [1,4].

Heroin: This substance is made of chemical compounds and its effect is three times that of morphine and it induces sleep. The addicted person is always dozing and has sleepy eyes [1,4].

Cocaine: It is a stimulating, hallucinogenic and delirious substance, those who become addicted to this drug usually develop sexual sadism and that is why they are very dangerous people. It escalates, its physical effects are few, while its psychological effects are more than heroin [1,4].

LSD: The consumption of these substances does not cause physical addiction, but it has harmful brain and psychological effects, these substances are hallucinogenic and lead to psychological addiction [1,4].

Amphetamines: Amphetamines are stimulant and addictive substances. These substances stimulate the central nervous system, these substances are used more among students because they cause sleeplessness and put a person in a stimulating state. Consuming these substances makes the body resistant to them, so the addicted person must consume more [1,4].

Marijuana and Hashish: Consumption of these substances does not cause physical addiction, but they cause mental addiction and therefore they are harmful, consumption of these substances has unpleasant brain effects, and they are often consumed in the form of cigarettes. Its harmful effects: relaxing sleep, intensifying feelings, unnecessary and long laughs, the pleasure of time and place, but when the effect of the drug ends, the addicted person feels bad and the possibility of committing a crime increases, and on the other hand, it is a factor for the consumption of stronger drugs such as heroin [1,4] (Figure 2).

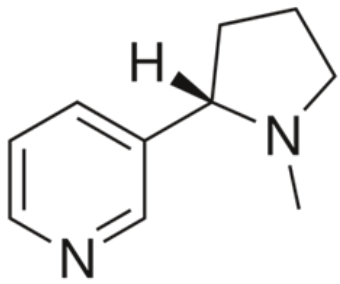

Figure 2: Schematic of the cyclic structure of nicotine [1].

Methadone: It is a narcotic drug that is used for the treatment of addiction due to its long half-life of more than 24 hours and should be prescribed only in addiction treatment centers and by a doctor [1,4].

Inhalants: This group includes various chemicals that evaporate quickly. Unlike other substances of abuse that are classified based on the effect they have on the central nervous system; these substances are placed in a group based on the common way they are used. Inhalants are divided into three categories based on their pharmacological function: volatile solvents, nitrous oxide, and nitrites. The first group, i.e., volatile solvents, are the most abused inhalants. All types of fuels such as gasoline, diesel, and lighter gas, anesthetics such as ether, adhesives, sprays, chemical dyes, etc. are included in this group [1,4] (Figure 3).

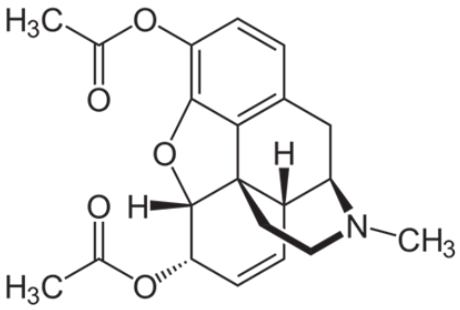

Figure 3: Schematic of the cyclic structure of heroin [1].

Chronic Addiction

Not everyone who uses drugs is considered an addict. Those who consume drugs are divided into three categories, but among them only chronic addicts are diagnosed with addiction disease [1,5].

Tefna Consumer:

a. Sometimes he uses drugs for fun and on special occasions.

b. He feels euphoric and doesn't overdose - he has a normal reaction to substances.

Heavy Consumer:

a. He uses drugs to help him cope with the stress and pressure of life.

b. He uses drugs to escape painful feelings.

c. They gradually increase their consumption and as a result, their body's resistance to substances increases.

d. He feels restless when the material is not available.

e. The beginning of experience in the process of physical and mental deterioration.

f. The beginning of the disorderly process of educational or occupational status.

g. The beginning of the process of losing interest in simple pleasures.

h. The beginning of the tendency to seclusion and isolation.

i. A heavy user has the power to control or stop using drugs as soon as they have a reason to quit.

j. A heavy user can become a heavy user or a real addict [1,5].

Chronic Addiction

a. Chronic addicts can never return to the state of heavy or heavy users.

b. Drug addicts feel great pleasure and relaxation from using drugs.

c. The brain gets used to using drugs and becomes dependent on drugs to function normally.

d. The structure and communication system of the brain becomes abnormal.

e. Loss of sanity and nervous and violent behavior.

f. Being unable to quit drugs despite the dire consequences, this condition is called allergy.

g. The brain needs drugs more and more, such a state is called Viyar phenomenon.

h. To get the previous feeling of pleasure, he must always consume more drugs, the body's resistance increases.

i. Ignoring and neglecting oneself and others.

j. Loss of connection with friends, family, and society.

k. Inability to do normal work and activities.

l. Get into legal trouble.

m. The disease of addiction has developed and has become advanced.

n. He needs drugs for normal daily activities.

o. Drugs are prioritized over other issues.

p. Losing interest in life and thinking about suicide.

q. A hangover when the substances needed by the body are given less than usual or completely cut off.

r. Continuous but futile attempts to get rid of addiction.

s. Chaotic and unmanageable life.

t. Complete despair and helplessness [1,5].

Side Effects of Addiction

Addiction to drugs, in addition to the losses it has directly for the user, and no benefits or benefits have been confirmed for its use, is one of the main factors in the spread of diseases such as AIDS and hepatitis, and also has heavy social and economic losses for the society. Among them, we can mention the destruction of a part of the force and the active brain of the society. One of the most important harms that drug use has on a person's health is a long-term decrease in sexual power. Although some drugs increase libido and arousal in the moment, most of them reduce sexual power in the long term. For example, the use of methadone causes a decrease and loss of sexual desire, erectile dysfunction and ejaculation disorder. About 75% of methadone addicts complain of decreased or lost libido. About 70% have sexual arousal problems and 60% have problems achieving sexual satisfaction [1,6]. Recently, some have modeled addiction using economics to show how much today's income and drug use will affect future drug demand [1,6].

Symptoms of Addiction

According to the definition of the American Psychological Association, if at least three of the following symptoms appear in a person who uses drugs in a 12-month period, the person is diagnosed with an addiction disease. These symptoms include: the body becoming more resistant or tolerance, the temptation to consume, increasing consumption, losing control over the amount

of consumption, continuing to consume despite the dangerous consequences, and the appearance of hangover symptoms in case of non-consumption [1,6].

The Effect of Addiction on the Psyche of the Family

With the presence of an addict in the family, the lives of all members are affected in some way. Family members are forced to make changes in their lives to cope with the devastating effects of addiction. Over time, this method causes them to face many problems in their lives. Although drug addiction has always been more among men than women, but in the last few years, there has been a significant increase in addiction among women in Iran. Based on the studies and research conducted in the field of women's addiction, women are caught in the trap of addiction due to insufficient information and ignorance. Also, the head of the country's welfare organization stated that more than 50% of addicts are married people, stating the increase in addiction among women in the country [1,7].

There are a series of devastating emotions and feelings that endanger the mental health, behavior, and quality of life of family members due to living next to an addict. Such feelings and behaviors include:

Feeling of Guilt

The state in which family members think that they are to blame for their loved one's addiction.

Anger

Includes anger from the addict and his unpredictable behavior or anger from the causes and factors that caused his addiction.

Denial and Feelings of Shame

Families who do not have enough knowledge about the disease of addiction try to deny or always feel ashamed to escape the disappointment and shame of their loved one's addiction.

Anxiety and Worry

A condition that occurs due to the unpredictable behavior of the addict, and numerous events that result from the consequences of the addiction of one of the family members and causes the family members to always live in anxiety and worry [1,7].

Contribution of Genetic Background in Human Addiction

Epidemiological studies clearly state that genetic factors are involved in all stages of addiction, including the beginning of vulnerability, continuous consumption, and tendency to dependence. The World Health Organization has estimated that there are 2 billion alcohol users, 1.3 billion tobacco users, and 185 million illicit drug users in the world [1,8].

In recent years, significant progress has been made to identify genes that predispose to addiction. Studies show that there is a high possibility of regions in chromosomes 4, 5, 9, 11, 17 as shelters for genes predisposing to addiction to various substances. Among these candidate genes for addiction susceptibility, we can mention aldehyde dehydrogenase (ADH), nicotinic acetylcholine receptor units (nAChR), GABA receptor subunit 2 (gamma aminobutyric acid A) or GABRA2, ANKK1, and neuroxin. So far, more than 1500 genes associated with human addiction have been identified. By examining the genetics of congenital addicts, the researchers found that there are changes in some alleles that make up genes prone to addiction in these people, which are not observed in healthy people [1,8] (Figure 4,5) (Table).

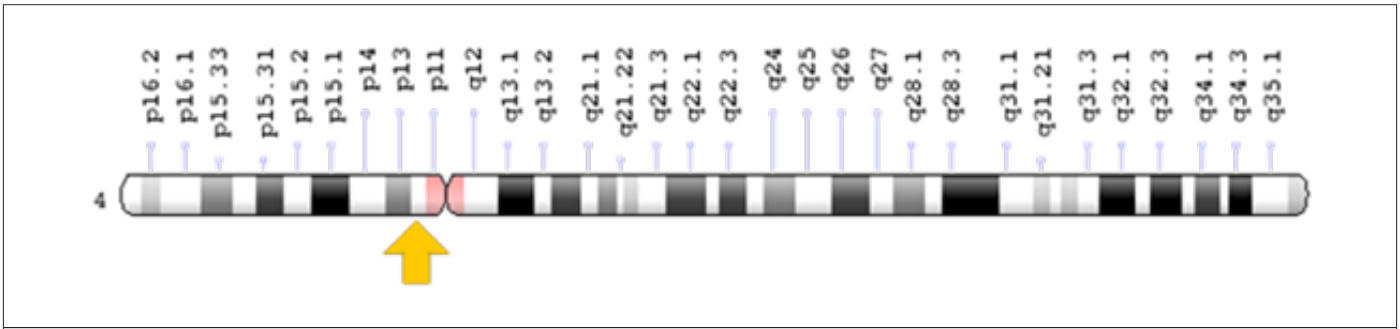

Figure 4: Schematic view of chromosome number 4, where the GABRA2 gene is located in the short arm of this chromosome as 4p12 [1].

Quantitative Genetics in Addiction-Susceptible Twin Studies

Twin studies are used to investigate the contribution of genetic and environmental factors. In addition to estimating genetic susceptibility, twin studies provide information on the contribution of environmental factors including availability or exposure to a substance and specific environments [1,9].

Many twin studies for alcohol-related behaviors have shown that the heritability of alcohol abuse and dependence is about 50-70%. Meta-analysis of twin studies has determined that both gene and environmental factors are important in smoking-related behaviors, and the heritability is estimated at 50%. Genetic factors in women play a greater role in the initiation of drug use than the continuation of its use. On the contrary, it is seen in men [1,9].

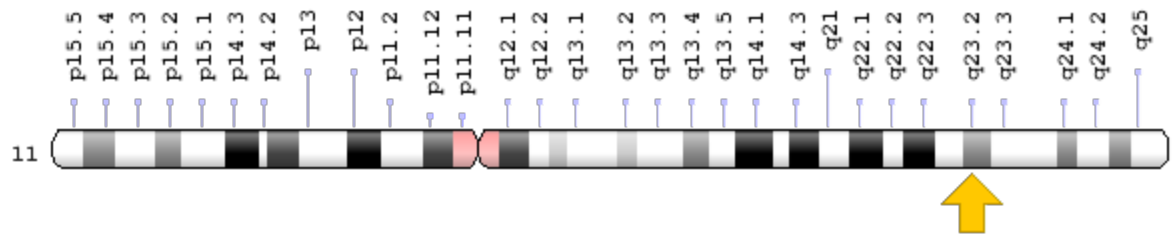

Figure 5: Schematic view of chromosome number 11, where the ANKK1 gene is in the long arm of this chromosome as 11q23.2 [1].

Table: Some candidate genes and their polymorphisms involved in human genetic addiction [1].

Gene	Locus	Altered Allele	Polymorphism Number	Altered Allele Frequency
OPRM1	6q25.2	A/G	rs1799971	0.14
		G/A	rs9479757	0.08
		T/C	rs3778151	0.15
		G/A	rs510769	0.25
OPRD1	1p35.3	C/T	rs2236861	0.29
		T/G	rs1042114	0.11
OPRK1	8q11.23	G/T	rs1051660	0.08
ADRBK2	22q12.1	G/A	rs5761122	0.29
STAT6	12q13.3	T/C	rs841718	0.47
COMT	22q11.21	G/A	rs4680	0.49
MC1R	16q24.3	C/T	rs1805007	0.05
		C/T	rs1805008	0.07
UGT2B7	4q13.2	T/C	rs7439366	0.43
ABCB1	7q21.12	C/T	rs2032588	0.07
		G/T/A	rs2032582	0.40 (T)
		C/T	rs1045642	0.02 (A)
				0.48
SLCO1B1	12p12.1	T/C	rs4149056	0.15
		T/C	rs2306283	0.35
SLCO1A2	12p12.1	A/C	rs11568583	0.07
		A/T	rs45502302	0
GAL	11q13.2	A/G	rs948854	0.23
HTR1A	5q12.3	C/G	rs6295	0.49
DRD2	11q23.2	C/T	rs6275	0.32
		T/C	rs6277	0.43

Researchers in a small number of studies have also tested genetic effects in drug addiction. The heritability of consumption and addiction to alcoholic beverages, sedatives and heroin in men is: 0.33, 0.27, 0.54 respectively. It is worth noting that these values are like those observed in women, but such studies are rare. For example, based on twin studies, the influence of genetic factors in nicotine addiction is about 33-71% and in cocaine addiction is about 42-79% [1,9].

In addition, studies show that the ADH2 gene increases the susceptibility to alcoholism in American Indians and whites. One of the most successful examples of local candidate gene studies in addiction susceptibility is the identification of the GABRA2 gene as a susceptibility factor for alcoholism. In addition, CHRNA4, CHRNB2, CHRNA5/A3/B4, ANKK1 genes are also effective in human addiction to alcohol, nicotine, and cocaine [1,9].

Conclusion

One of the traditional addiction tests is the urine test, which is not a certain and accurate method, and a person can change the test result by using special chemicals, although there are other methods for addiction testing that can be used with high confidence. Considering the nature and structure of addiction, it is very important to pay attention to the psychological aspect of this disease. Therefore, tests and experiments are also available to find out the addiction status of a person according to their behavioral and psychological aspects, which include questions that the person must answer [1-10].

There are different ways to treat addiction, each of which can produce different effects depending on the addict. But it can be said that almost all researchers have concluded that behavioral therapy can be the most effective method to treat addiction. By making a change in the person's attitude, the therapist will be able to stop the person from using drugs and discourage him from returning to drug use. Matrix is one of the first methods of addiction treatment. The "Matrix" model was supposed to be a 16-week program that included individual therapy sessions, group therapy, illness therapy, family therapy, education, and encouragement. Management is also one of the important components of this method. This management is in the form of reward for non-use and non-punishment for return and use [1-10].

Just as the patient cannot be expected to stop it with willpower, the addict cannot be expected to overcome his addiction with willpower. He needs medical care and the wise, compassionate, and patient support of those around him. Just as if he had a fever as a child, family members would treat him until he fully recovered, now he needs such care. Even after hospitalization and quitting, it is necessary for the family to take care of him for a few years, if he returns to drugs again without blaming him, they should patiently help him quit again and continue to take care of him. Just as a heart patient needs care, an addict whose brain is sick also needs special care. In addition, in this type of disease where the biochemistry of the brain is affected, the person is not able to learn from his past experiences and so to speak, connect the dots of cause and effect, in fact, until several months after quitting and detoxing the body. The patient cannot be expected to speak yet. Because he listens to advice but does not analyze and understand. He is not even aware of his own situation. Expecting him to understand his situation in such a situation is like expecting a broken computer to send a message that it is broken. The family should also pay attention to their sick friends; Do not allow some people to create temptation to thwart his efforts to improve. As the saying goes, the first step to staying safe from a storm is to close the doors and windows. For this purpose, it is necessary to establish a sincere relationship with the patient so that he can be informed about the existence of such tempters and then help him to avoid meeting with them [1-10].

A new study shows that the desire to use drugs exists in addicted people even after death. There is a protein in the reward center of the human brain that is chemically altered, shortened, and split in drug addicts. Austrian researchers have found, based on multiple autopsies, that an altered protein in heroin addicts shows that cravings for the drug persist even after death. This protein, called FOSB, is a transcription factor in the brain that, along with other molecules, is involved in signal transmission (transmission of stimuli to the cell). This protein is said to be responsible for transferring genetic information between cells, as well as determining whether certain genes are activated [1,10].

FOSB is part of the active protein AP-1, which is involved in the regulation of gene expression in response to a wide range of stimuli, including stress and bacterial infections. Due to the continuous use of drugs such as heroin, FOSB has turned into Delta FOSB, which is increasingly stimulated in the brain in cases of chronic use and even penetrates the growth factors and causes structural changes (neuroplasticity) in the brain and the area of memory formation. Evidence obtained by the University of Medical Sciences of the Ministry of Forensic Medicine in Vienna shows that this modified protein is still active even after death in addicted people. They reached this conclusion by examining tissue samples from the nucleus accumbens (an area of the brain) of 15 deceased heroin addicts [1,10] (Figure 6).

Using highly accurate diagnostic methods, the researchers found that Delta FOSB was still detectable up to 9 days after death. Although mutations in this protein can be detected more than a week after death in an addict, researchers believe that this period is much longer and can even take months for living people who are trying to quit. They also showed that these results can be effective in the treatment and management of people with drug dependence and heroin addiction. These researchers stated that the desire to use drugs remains in the addicted person for months, and for this reason, psychological care, and support for these people after quitting is very important [1,10].

Acknowledgment

None.

Conflict of Interest

No conflict of interest.

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