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Review Article

Substance Use and Abuse in Adolescents: The Contribution of Neuroscience and Psychology

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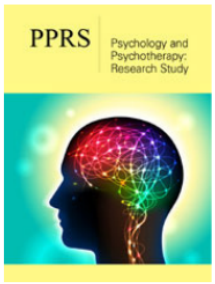

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Abstract

Data reported by the European Monitoring Centre for Drugs and Drug Addiction show a steady growth in the consumption of illegal substances, especially in adolescence. The scientific evidence shows results from the early use of narcotic drugs, which adversely interferes, both with the processes of development and brain maturation of the adolescent, and a high correlation has been found between psychopathological personality traits and psychiatric disorders in subjects taking psychotropic substances. The aim of this work is to review the data in the literature and offer a contribution that leads to reflection on preventive and educational interventions, to be activated for a population of subjects particularly at risk: adolescents. This means taking early action to promote normal personality development, to promote healthier lifestyles and thus to prevent future damage to physical and mental health.

Drugs and Addiction: The Phenomenon in Italy

The problem of drug addiction in Italy has become a social problem since the 1970s. In this period, use psychoactive substances takes on the connotation of rebellion and transgression, to the prevailing culture reflecting an alternative "counterculture" than the predominant one, Cannabis and "psychedelic" drugs, the so-called "hard" drugs, such as morphine and heroin, are also used. In the eighties and nineties, there was a progressive use of drugs and the growing emergence of HIV and social alarm, associated with this disease by drug users. In the 1990s, so-called "new drugs" such as cocaine and ecstasy appeared on the market, they are considered attractive because of their ease of use and their stimulating effects, and there is a misperception of their effects, as they are also addictive, compared to heroin, consumption also increases dramatically being predominantly consumed in entertainment, sports and workplaces. Thus, arises polyassumption, in which the abuse of the main substance, usually heroin, is accompanied by the use of other psychotropic substances such as cocaine, cannabis, alcohol and benzodiazepines.

Today's scenario is characterized by the logic of drug distribution that chases the continuous changes in the market, with internet technology playing a leading role in facilitating the availability of substances. The products are increasingly varied and characterized by low prices; the sale follows increasingly diversified channels» [1]. The Annual Report to the Parliament on the Phenomenon of Drug Addiction in Italy for the year 2023 provides a complete picture of the complex situation of drug addiction in the country [2-15]. From the point of view of consumption, there has been an increase in the phenomenon in different age groups: in the 18-84 age group and in the 15-19 age group. However, the increase observed among young people, compared to the 2021 data, is particularly worrying: there is a significant increase in consumption in the youth group, rising from 18.7% to 27.9%. This increase is particularly marked in the use of synthetic cannabinoids and new psychoactive substances.

As regards the impact on health, there is a general growth in the use of public services and therapeutic communities by people involved in drug addiction. At the same time, there is an increase in cases of access to emergency rooms and hospital admissions related to drug-related

issues. Relevant is also the increased diagnosis of HIV and AIDS infections, often in an advanced stage. This must make us reflect and focus on the need for greater efforts in the field of prevention and information. Another change in trend is related to the gender (male and female) of people involved in drug addiction, an analysis found that 15- 16 years-old female students have prevalences of use comparable to or even higher than those of male peers in the use of cannabinoids, new psychoactive substances, cocaine and opiates. This phenomenon is also detectable in the adult population, with an increase in the prevalence of consumption in women.

Cocaine retains its relevant presence in the drug market in Italy, with a significant amount of the substance arriving mainly by sea from the producing countries of South America. Data from 2022 show that in Italy more than 26 tons of substance have been seized, compared to about 3 and a half tons in 2018. It is widely used by young people [15-19]; there are about 44,000 students who report its use (about 2% of the student population). During the same year, the use was recorded by about 500,000 individuals, aged between 18 and 84 years, representing 1.1% of the population. Cannabis derivatives are the most common drugs in Italy. In addition, during 2022, 9,400 police operations, which make up about 50% of the total operations, were confiscated more than 47 tons of cannabis and its variants. The widespread spread in the country is further confirmed by the fact that about 4 million people, between 18 and 84 years (8.5% of the population), have reported using cannabis products at least once during the year. Through waste water analysis, it is estimated that there are about 50 daily doses per 1,000 inhabitants.

In the student population, about 25,000 boys (1%) reported the use of the substance in 2022. In the general population, the number of people aged between 18 and 84 who reported using heroin/opiates at least once in the year has increased significantly, reaching 750,000 people (1.4%). This value is three times higher than in 2017. The particular characteristics of the New Psychoactive Substances (NPS) make the monitoring of their diffusion extremely complex. In the general population, about 300,000 people in 2022 reported using NPS. Among the student population there are over 140 thousand children who report their use. In particular, the most popular NPSs among students are synthetic cannabinoids (4.4%), followed by synthetic opioids (0.9%), ketamine (0.7%) and cations (0.5%). (The new psychoactive substances are synthetic products that can be easily modified, rendering them undetectable and not immediately included in the lists of substances prohibited by international laws and agreements. This category is extremely vast and changing, constantly evolving, and includes high-risk or potentially deadly compounds.

Comparing data between Italy and other countries of the European Union, our country is among those with the highest percentages in Europe for drug use. Data from the European Report on Drugs of 2022, report that in 2019 in Italy the estimate of high-risk opioid use reaches 7.2-7.9 cases per 1000. This is the highest recorded figure. The lowest recorded is that of 2010-2011 in Hungary with 0.4-0.5 cases per 1000. For cocaine use, it is estimated that during 2017 in Italy 1.7% of young adults (15-34 years) used cocaine. In Turkey, in the same year (2017) the estimate of young adults who have used cocaine is 0.1%. Ireland in 2019 and Austria in 2020 have 4.8 and 5.6 respectively. Compared to cannabis use, 20.9 % of young adults in Italy in 2017 used cannabinoids throughout the year.

Defining

Etimologically, the word “drug” comes from the Dutch term “droog”, which means “dry” or “dried”, in the pharmacological field, instead, the term “drug” takes on a different meaning, indicating every substance from natural origin, both plant and animal, containing one or more active ingredients. These active ingredients, once properly extracted, prepared and preserved, are used for experimental therapeutic purposes. The World Health Organization (2023) gives an extended definition of the term: Psychoactive drugs are substances that, when taken or administered in your system, affect mental processes, such as perception, consciousness, cognition, or mood, and motion. [...] The production, distribution, sale or non-medical use of many psychoactive drugs are controlled or prohibited outside the channels legally authorized by law. Psychoactive drugs have varying degrees of restriction of availability, depending on health risks and therapeutic usefulness, and are classified according to a hierarchy of programs both nationally and internationally...»

The WHO definition suggests the main characteristics of the drug:

A. Substance

B. Amazing

C. Subject to the law

The drug is a “substance”, because it is composed of chemical elements; it is “amazing”, because it causes an alteration of the mind, mood and senses; it is “subject to the law”, because the use is controlled and limited, social order and crime prevention. Drugs cause addiction and represent a distortion of behavior that transforms a common habit into an excessive and pathological search for pleasure by means, substances or actions. The sensation of pleasure resulting from the use of narcotic substances appears initially rewarding, however it will tend to dissolve quickly, resulting in the need for new and higher intake of the substance.

According to DSM-5 [3], a pathological mode of use of the substance leading to clinically significant discomfort or impairment is characterized by at least two of the following conditions, occurring within a period of 12 months:

A. The substance is often taken in larger quantities or for longer periods than the subject intended.

B. Persistent desire or successful attempts to reduce or control the use of the substance.

C. A large amount of time is spent on activities necessary to procure the substance (e.g. visiting several doctors or driving

long distances), taking it (e.g. by smoking "in a chain"), or recovering from its effects.

D. Craving or strong desire or urge to use the substance.

E. Recurrent use of the substance that causes failure to fulfil the main obligations of tenure at work, at school, at home.

F. Continued use of the substance despite the presence of persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the substance.

G. Important social, work or recreational activities are abandoned or reduced due to the use of the substance.

H. Recurrent use of the substance in situations where it is physically hazardous.

I. Continued use of the substance despite awareness of a persistent or recurrent problem, physical or psychological, that has probably been caused or exacerbated by the substance.

J. Tolerance, as defined by each of the following: a) the need for significantly higher doses of the substance to achieve intoxication or the desired effect; b) a significantly decreased effect with continuous use of the same amount of the substance.

K. Abstinence, as manifested by each of the following: a) the characteristic withdrawal syndrome for the substance (refer to Criteria A and B of the set of criteria for abstinence from specific substances); b) the same substance (or a closely related one) is taken to alleviate or avoid withdrawal symptoms. »

L. With drug addiction, reference is made to the more specific condition of those who feel the irrepressible and frequent need to take a substance, despite the awareness of the harmful effects that it can produce» [4].

Classification of drugs

The categorization of drugs is based on the definition by the regulatory system, which is influenced by social, economic and cultural factors. The system determines whether drugs are considered legal or illegal; light or heavy; natural or synthetic. Their legality may also depend on therapeutic use, prior prescription of a doctor, as in the case of morphine. The effect of substances is also evaluated for the effect on the central nervous system.

In this respect, four broad categories of drugs are distinguished:

A. Drugs that depress the central nervous system.

B. Drugs that reduce pain.

C. Drugs that stimulate the central nervous system.

D. Drugs that alter perceptive function» [5].

Depressing drugs are alcohol, barbiturates, benzodiazepines, solvents. If used in moderation, these substances reduce anxiety and tension, concentration ability and memory, leading to feelings of well-being, relaxation and mild euphoria. Narcotics reduce pain, sensitivity and emotional reactions. They are derived from poppy,

Drugs stimulate amphetamines, methamphetamines, designer drugs, MDMA, nicotine, cocaine and lacaffeine. These increase alertness and attention, decrease the feeling of fatigue and hunger. The hallucinogens, finally, are marijuana, LSD, ketamine, mescaline, this act by altering the perceptive function, modifying sensory experiences thanks to illusions and hallucinations, and favoring states of euphoria.

In Italy, the rule on drugs is regulated by the Decree of the President of the Republic (D.P.R.) n.309 of 1990. National law lays down directives on the production, trade and use of drugs, as well as dealing with the fight against illegal activities, the prevention of drug addiction and the care of the people involved. Drugs are not classified according to their effects, but according to the presence within tables that are periodically updated by the Ministry of Health. The Italian Government in 2006 introduced the so-called Fini-Giovanardi Law, which unified sanctions for all violations, regardless of the type of narcotic involved. This law removed the distinction between soft and hard drugs, and all substances under the same legislation. However, in 2014, the Italian Constitutional Court declared the Fini-Giovanardi reform unconstitutional for procedural issues. As a result, the sanction differentiation between hard and light drugs has been restored. This distinction has been reaffirmed through the creation of five new tables, which also include substances introduced in 2006 or later.

Although in Italy, as in the rest of Europe and the world, most drugs are illegal, it is estimated that 4 million 900 thousand people living in Italy aged 18-84 years have taken at least one illegal drug during 2022 (demographic.adnkronos.com). The substance most commonly used in the same year by the same target was cannabis; followed by opiates and opioids, cocaine, stimulants, hallucinogens and New Psychoactive Substances (NPS).

Cannabis

Along with tobacco, alcohol and caffeine, cannabis is one of the most consumed drugs in the world. Two types of drugs are derived from cannabis: marijuana, which is obtained from the inflorescences and dried leaves of the plant, and hashish, resin extracted through various typing and pressing techniques, packaged in sticks and cakes; cannabis oil (hash) is instead extracted from cannabis by solvent. The active ingredient is Δ9-tetrahydrocannabinol - commonly known as THC - the substance responsible for the effects of cannabis on the body. The cannabis variety "indica" has calming and relaxing properties, while the cannabis "sativa" has an energizing and stimulating effect. The latter type is dioecious: there are, that is, male and female plants.

Cannabis is typically smoked, often mixed with tobacco or placed in a smoking device (bong). Alternatively, it can be eaten, receiving an effect that lasts longer. After taking cannabis, the effects reach their peak after about 10 minutes and last 1-3 hours. Such effects can vary from person to person, the effects usually experienced by people after taking cannabis are euphoria, lightheartedness, sensory changes, increased appetite, lack of coordination, difficulty in concentration and memory, increased heartbeat, anxiety and

and are opium, morphine and codeine, heroin and methadone.

paranoia, drowsiness, effects on blood pressure, vasodilation.

With cannabis some young people consume legal psychoactive substances such as alcohol and tobacco: this triad connotes the vast majority of fun-related consumption situations. The intake of cannabis is, therefore, reinforced by peers, and it occurs due to imitative processes or fears related to exclusion from the group and the lack of social integration. The practice of smoking individually develops when intentionality takes over, when the purchase of the substance is sought and its use is no longer accidental and occasional, but becomes habitual, continuous and compulsive» [5]. Gateway Theory (gateway theory) is based on the idea that cannabis users would be more likely to switch to other substances than non-users.

Cocaine

Cocaine appears to be, after cannabis, another illicit substance frequently used throughout Europe. The coca plant is native to South America, mainly Peru, Colombia and Bolivia are obtained by grinding coca leaves. Cocaine commonly sold on the market is rarely pure; it is often mixed with other substances, including talc, caffeine, anesthetics, amphetamines or heroin. Cocaine is taken by inhaling, after passing through the nasal mucous membranes, the substance enters the bloodstream, and the effects manifest themselves within a few minutes, then vanish within half an hour. Cocaine can also be used by smoking it with pipettes or intravenously, even mixed with other substances, such as heroin.

Once it reaches the brain, cocaine begins to produce the effects, inducing in those who use it a strong feeling of euphoria, with improved cognitive and motor performance, increases hypervigilance and decreases the desire for food and sleep. The feeling of greater well-being leads the subject to a reduced perception of risk, resulting in risky attitudes in situations of potential and high danger. On a physical level, it increases the heartbeat, blood pressure, body temperature, and the pupils dilate. These effects remain present for a relatively short period of time, usually between 15 and 90 minutes followed by dysphoria, the so-called "down", in which feelings of sadness, apathy, difficulty of concentration and attention are present, agitation, nervousness and fatigue. Faced with the "down", the individual often responds by looking for another dose in order to mitigate the effects.

Cocaine, in the 1980s, was reserved for some of the wealthier classes, but is now widespread among the general population and among young people, regardless of income, profession, culture and age. There are two groups of habitual consumers. The first is made up of socially integrated consumers, who use the substance on weekends, at parties, on special occasions, sometimes in large quantities or frequently. Many claim to control consumption by imposing rules, although compulsive patterns of use are often developed that require therapeutic intervention. The second group includes the most marginalized or socially excluded consumers, including former consumers of heroin that may use crack or injecting cocaine» [5]. Crack, unlike cocaine, is defined as the drug of the marginalized. It is a substance derived from the processing of cocaine, with the addition of sodium bicarbonate and ammonia. It is used through special pipes and this mode of intake produces

15 minutes). The effects sought include sensations of energy and strength, improved communication ability, euphoria, decreased inhibition, increased vivacity and a sense of strong excitement. However, the down is very heavy.

Heroine

The commercial name "heroin" comes from the German "heroish", which means "heroic", since it was a substance recognized as an analgesic superior even to the effectiveness of morphine. Until the 1920s, heroin could be purchased in pharmacies as an analgesic. It was subsequently banned from trade when it was found that, in addition to the common headaches and coughs, it had long-term devastating effects on the human body, as well as morphine had greater side effects, including the high risk of addiction. The use of morphine to date remains reserved for the treatment of painful syndromes such as cancer pain, severe trauma, etc. Heroin is a semi-synthetic substance obtained from the chemical processing of morphine, which in turn is obtained from opium, a substance extracted from the seeds of certain varieties of poppies. Heroin is presented as a very fine powder, typically white in color, but can also be brown or reddish depending on purity. Production, in fact, can be subject to a number of cuts with other dangerous substances.

Heroin can be snorted, smoked, injected into the vein. The effects vary depending on the mode of intake: intravenous injection produces more intensity and a rapid achievement of euphoria (7 to 8 seconds), while intramuscular injection produces a relatively slow onset of euphoria (5 to 8 minutes). If inhaled or smoked, the strongest effect is generally between 10 and 15 minutes» [6] Heroin users report that they quickly experience a series of pleasant sensations, commonly described as a "rush" (rush), shortly after taking the substance. The intensity of these sensations depends on the amount of drug taken and how quickly it enters the bloodstream. Such pleasant effects have an extremely short duration of only a few minutes. The immediate results of taking them are therefore pleasant.

This rush phase is followed by a « phase characterized by calm, relaxation, satisfaction and detachment from what happens outside» [7]. About an hour after taking, you reach the peak of the heroine's effects, the mind can perceive a feeling of deep tranquility and the body can be enveloped in a kind of intense and inner pleasure. In this state, it is common for the consumer to seek isolation to fully enjoy these sensations, often temporarily forgetting any problem or concern. After the initial effects, the users remain dormant for many hours. The mental functions are clouded by the effect of heroin on the central nervous system, which also leads to a lowering of heart rate and breathing, which decreases enormously, sometimes to the point of causing death. The effect is exhausted within 2-6 hours of injection» [7]. After the initial euphoric effect wears off, a number of characteristic symptoms emerge, including clearly narrowing of the pupils ("spiked pupils"). This is accompanied by a feeling of drowsiness, apathy and difficulty in maintaining concentration. Physical and mental activity decreases, and language may appear confused and fluid. You may experience an insistent itching and may experience nausea that can result in vomiting

a rapid increase in effects, which are intense but short-lived (3-

Neurobiology of Drug Dependence

The abuse of psychotropic substances and the development of pathological dependence can generate adverse health effects both in the short and long term. The effects of drugs do not mimic physical impact, but can also affect psychological balance, financial stability, personal relationships and social interaction. Substance abuse has consequences for the brain. In the previous section we gave the definition of the disorder from use of substances and the symptomatology through which it manifests, we review the neurobiological mechanisms that intervene.

One of the main brain systems involved in the dependence process is the limbic system, which it also has the function of regulating and controlling visceral states, emotions, cognition and behavior, and is involved in modulating the activity of the autonomic nervous system and in the formation of memories, takes part in the process of regulating emotions and motivated behaviors, including struggle, flight, nutrition and sexuality [8]. One of the key neurotransmitters in the limbic system is dopamine, which directs motivated behavior. Two other neurotransmitters worthy of note are serotonin, which seems to modulate the release of dopamine, and norepinephrine, involved in arousal and physiological activation [9].

The intake at high doses of narcotic substance makes the subject experience an intense state of pleasure, resulting from the increase of dopamine in the regions of the limbic system, in particular in the nucleus accumbens, the immediate well-being experienced, acts as a reinforcement and is encoded in memory as a positive moment, this process gives rise to a learning mechanism by conditioning, in which amygdala and hippocampus are involved [10]. Repeated intake of substances serves as a positive incentive. Robinson & Berridge [11] with the theory of incentive-sensitization claim that repeated exposure to the drug can, under certain circumstances and in susceptible individuals, make the dopamine system hypersensitive not only to the effects of the substance, but also related stimuli.

The craving is thus associated with the learned response that connects the drug and its environment to a pleasant experience, resulting in a vicious circle that leads to addiction and consequent functional change of some brain circuits. The intake of the substance of abuse, would increase the neurotransmission of dopamine in the regions of the limbic system, chronic use would instead be responsible for a significant decrease in dopaminergic activity, persistent also after detoxification and would also cause dysregulation of the frontal areas of the brain, in which they are implicated, the orbitofrontal cortex, involved in the evaluation of stimulus salience, and the anterior cingulate gyrus, involved in the inhibitory control of impulses [12].

At the level of the orbitofrontal cortex there is a decrease in sensitivity to natural reinforcements, the substance being a very high positive reinforcement, the individual does not take pleasure in daily activities experiences a state of anedonia that can be alleviated only by taking the substance. Neuroimaging subjects. In dependent subjects not in abstinence, she was found to be overactive in response to the drug or related stimuli [12]. The hyperactivation of the orbitofrontal cortex determines an activation of the underlying reward circuits involved in the craving experience and which in turn would contribute to a strong reduction of inhibitory control exercised by the frontal cortex and in from the lap of the front track, structures already compromised. The decreased activity of the frontal cortex would be associated with a decrease in serotonin transmission, which is unable to regulate the dopaminergic activity of the subcortical areas of the limbic system. All this implies a difficulty in inhibiting the drive for drug research and consumption. The impairment of inhibitory processes determines the transition from impulsive to compulsive intake, the individual assumes the substance even when there will be no response as to initial well-being. Not all drugs act in the same way on the nervous system and not all produce the same effects.

Dopamine at the nucleus accumbens is released following appetizing stimuli (which determine motivation) and new, salient or unexpected consumer stimuli. Most psychotropic abuse substances (alcohol, heroin, marijuana, benzodiazepines, cocaine and amphetamines) and environmental stimuli such as food, sexual activity, play, determine an increase in dopaminergic transmission at the level of the shell region of the nucleus accumbens; (considered the mechanism behind the gratification and strengthening effects of abuse substances) [13]. Abuse substances allow the release of dopamine to a greater extent and prolonged, compared to natural stimuli. In particular, both cocaine and amphetamines act directly on dopaminergic neurons, blocking the Dopamine Transporter (DAT) and increasing the neurotransmitter at the synaptic level, this effect is also achieved after repeated administration, in this case you will encounter habit and the release of dopamine will gradually reduce.

Imaging Studies

Advances in neuroimaging methods (functional MRI, PET and SPECT) have allowed in recent years to study changes in specific brain areas in relation to behavior; PET has been used to assess the acute effects of substances on neurotransmitters such as dopamine, GABA and opioids; functional MRI to assess the degree of activity of specific brain areas in subjects affected by a condition of dependence during the different stages that characterize dependence (intoxication, craving and abstinence); the prefrontal cortex, the amygdala, the hippocampus and the nucleus accumbens are the brain areas that seem to be more involved in the development and maintenance of dependence [13].

Studies with PET and SPECT have shown that at the striatal level in substance dependent subjects there is a reduced concentration of D2 dopamine receptors and a reduction in dopamine release. This has led some researchers to hypothesize that dependent subjects have, because of this deficit, a lower sensitivity to natural strengthening stimuli [12]; therefore, the gratification circuits are more easily activated by substances, whose recruitment will be privileged over the search for natural rewarding stimuli. While the acute intake of the substances causes an increase in dopaminergic

studies show the hypoactive orbitofrontal cortex in abstinence

acute intake of the substances causes an increase in dopaminergic transmission, chronic consumption would determine a reduced

dopaminergic functionality that causes a dysfunction of the orbito-frontal cortex and cingulate gyrus [12].

These areas of the brain are implicated in the attribution of salience to stimuli and inhibitory control over dysfunctional behaviors. The reduced dopaminergic transmission, at the level of the orbitofrontal cortex and cingulate gyrus, could explain the altered functionality of control systems and the attribution of salience, which translates into compulsive research of the substance by dependent subjects [12]. These authors pointed out that these areas are hypoactive during abstinence, they are activated when the subject takes the substance, when he is exposed to stimuli related to the substance and when he experiences a strong desire for the substance. The greater the desire for the substance, the more intense will be the activation of the above areas. It has been shown that increased activation of these regions also occurs in compulsive behaviors, therefore, it could be the basis for the inability to exercise inhibitory control over the intake of substances and the implementation of substance-dependent testing [12,14] frontal cortical regions, are essential for executive functions in that they imply the ability to take decisions, to judge the consequences of one's actions and to exercise control over behavior.

Pathological Addictions: Mechanisms

When we talk about addiction, we refer to the compulsive need to take a chemical or a drug. The English terms "dependence" and "addiction" are both translated, in Italian, with a single term "dependence"; however, these English terms refer to two different phenomena: the first indicates the physical dependence on the substance that the body needs in order to function; the second indicates, instead, psychological dependence on a pleasant stimulus. A subdivision of addictions that is based on social regulators is due to Francisco Alonso-Fernández [15], who distinguishes "social or legal addictions" that include legal drugs (such as alcohol, drugs, tobacco, etc.) and socially accepted activities (such as eating, working, shopping, playing), "antisocial or illegal addictions" that include drug addiction and illegal activities (such as cocaine, heroin, cannabis, non-consensual sex). In this work, we will examine only addictions to substances.

From a symptomatological point of view:

A. The individual is unable to control his or her behavior by acting compulsively, which gives him or her pleasure.

B. Manifestly craving, defined as " an attraction, of varying intensity, to certain psychotropic abuse substances (...) at high levels of intensity, intense and serious psychophysical alterations appear that lead the subject to think only about the substances from which he is attracted and the means by which to obtain them".

C. May develop abstinence in the absence of the object of dependence and tolerance, which means that the rewarding effects of repeated use of the same dose of the substance or the compulsive implementation of an activity are reduced, and consequently, the individual is forced to increase the dose or

D. The individual persists in his behavior despite the negative consequences it entails. Several studies have shown that an excessive intake of substances provokes the activation of the brain system of reward: when the subject puts into action a behavior that causes pleasure and gratification, such a system is activated, resulting in a strengthening of the behavior itself, as it is encoded in the memory as positive.

In drug addicts there is an increase in the activity of the mesolimbic dopaminergic system, in particular dopaminergic neurons that originate in the ventro-tegmental brain area with projections to the nucleus accumbens. This increase in dopamine, a neurotransmitter that belongs to the catecholamine family and released by the brain when we experience gratification, determines the intense desire for the substance, considered indispensable to function and survive, encouraging the compulsive research of the same, in order to maintain the effects produced by it [16]. A malfunction of the brain mechanisms involved in gratification and motivation involving the meso-cortico-limbic circuits, seems to be the basis of both substance and behavioral addictions.

The regulation of these mechanisms is made possible by the interaction of different neuro transmitting systems; in particular, in addiction a crucial role is played by the dopaminergic system, which regulates the motivation that guides the search for rewarding stimulus [13]. Dopamine produces different effects on motivated behaviors depending on how it reacts to two different motivational stimuli: appetitive stimuli, which push the individual to get a reward, and consumer stimuli, that keep the subject's proximity to the reward. Both stimuli activate the dopaminergic neurons of the mesocortical pathway; while the dopaminergic neurons of the mesolimbic pathway, considered the pleasure pathway, are activated only by consumer stimuli.

In addition to the dopaminergic system, other systems involved in addiction mechanisms are:

A. The opioid system, which would mediate the processes of gratification resulting from the use of substance [13]. It has been observed, in fact, that gambling, sexual activity or compulsive eating behaviors are able to activate the release of endogenous opioids.

B. The serotonin system, the alteration of which seems to be related to impulsive behavior, typical of addiction.

C. The noradrenergic system modulates the dopaminergic system.

Robinson & Berridge [17] developed the theory of incentive sensitization, according to which repeated exposure to substances, in susceptible subjects and in certain situations, it would cause a modification and therefore a hypersensitivity of the brain circuits involved in the motivation mechanisms; consequently, the substance but also the mental representations related to it assume an incentive salient value, resulting in an increased desire (wanting) to take the substance. The authors of this theory believe that the craving phenomenon and relapses are based on the

activity to achieve the initial effect.

modifications of both synaptic plasticity in the nucleus accumbens and cortex and neurotransmitter systems such as serotonin, glutamate, norepinephrine and GABA (18)

Individual Vulnerability: Factors That Lead to The Development of a Pathological Dependence

During adolescence people come into contact with this reality, but not all those who start taking drugs can develop an addiction as their use can be limited to "occasional consumption". There is an individual vulnerability, called neurological or psychological susceptibility, that can promote the development of an addiction and the use of narcotic drugs in adolescence, this is caused by an evolutionary immaturity of the brain, which causes vulnerability to neurological changes resulting in a reduction in the individual's cognitive abilities. The use of substances in adolescence involves a marked interference with the processes of maturation and brain development, affecting different cognitive functions, such as learning, memorization, coordination and reward systems [19].

From epidemiological observations and sociological studies in the literature, we can see that there are individuals who, due to their individual, environmental, family or social characteristics, develop a condition of greater vulnerability. The factors that contribute to pathological dependence can be biological factors, psychic factors, social factors or environmental factors. The biological predisposition is one of the main risk factors because once the body comes into contact with the substance, there is a process that progressively binds the person to the psychoactive substance to be involved is the circuit of reward or gratification as there is an alteration in the production of endogenous neurotransmitters, dopamine, so if tested the pleasant experience generated by the substance, the subject is led to replicate it until the same reward circuit no longer responds to so-called "natural" stimuli So it needs the drug continuously to be activated [20].

Other factors that contribute to the establishment of a pathological dependence can be the socio-economic situation in which the subject lives (economic disadvantage, poverty); the co-existence of mental disorders for which the subject uses substances to manage motions; environmental factors such as the ease of finding substances; exposure to traumatic or stressful events such as child abuse or a problematic family situation; social factors such as the influence of the peer group. Also useful are prevention projects through sport, which have proven to be effective in the prevention of risk behaviors: sport is in fact a tool for the promotion of well-being that strengthens relational skills and social skills, sport is an important element both from the educational point of view and in terms of building a balanced personality. Through constant educational and psychological support, interventions can be implemented that recall the concept of resilience understood as the ability to face events in a positive way and to reorganize positively in the face of difficulties.

The phenomenon of pathological addictions and consequences on the development of adolescents, cannot be addressed, without taking into account the reference context within which they have developed and it is important that the actions implemented respond to the real needs of the subjects to which they are addressed. It is necessary in addition to traditional policies that are mostly based on the dissemination of information, to move to an approach that involves the direct involvement of the target audience. It has been shown that the development of pathological dependence is one of the consequences of a discomfort experienced during childhood [21].

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