

Drugs of Abuse – The Myth of Creativity and the Reality of Destruction

E. SYLVESTER VIZI

Institute of Experimental Medicine, Hungarian Academy of Sciences,
42 Szigony str., 1085 Budapest, Hungary. E-mail: esvizi@koki.hu

In every culture, man has used drugs to dispel anxiety, stimulate productivity, and to increase the feelings of joy and satisfaction. Drugs have also had an undeniable influence on art and culture. These substances become referred to as ‘drugs of abuse’ if their repeated consumption is triggered or induced by psychological or physical compulsion, often leading to conflict with society, either due to neglect of family or social duties, and also to criminal activities in order to obtain the materials. Drug abuse particularly affects young people and has become one of the most important and widely discussed issues in society. It is therefore an important task in medical science to find answers to how drugs exert their effect and what leads to addiction and permanent consumption.

Introduction

Throughout history, every society has used drugs that alter mood, thought and feelings. Humankind has always been looking for substances that make us feel good (or better) about ourselves. We want to escape the clutches of feelings of anxiety, disappointment, oppressive memory, and regret. The pursuit of happiness has always been an important question. Alas, the currently available drugs to change our mood and alter memory may have both positive and negative effects. Marijuana, cocaine, ecstasy, and other consciousness-affecting drugs offer temporary pleasures and escapes but may produce physical and behavioural dependence. The report of the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) treats the issue of drugs as a worldwide problem. Research carried out by the EMCDDA shows that the number of drug users worldwide is about one billion, meaning that nearly every sixth or seventh person in the world takes drugs that may lead to dependence. Hundreds of millions of people are

addicted to opium or opium derivatives (heroin, morphine) and cocaine, but cannabis is the most widely used illegal drug in the Western world;¹ it is estimated that there are some 350 million regular users. Three hundred million people chew coca leaves that contain cocaine, or qat leaves that contain ephedrine (in Ethiopia and Yemen) – drugs that are also part of the world’s medical heritage. The term ‘drug abuse’, as used in the literature, only refers to the use of illegal drugs, but excludes alcohol or medicines that are legally available on prescription.

From the Dance of the Medicine-man to Drug Crimes

Ever since man has lived on Earth, accidents, diseases and injuries have adversely affected people’s moods, naturally leading to the attempt to find remedies for grief, sorrow and pain. The knowledge of the medicinal properties of certain herbs was passed on from generation to generation, distinguishing healers, medicine-men, shamans, and herb-women from other members of the tribe or the village community. These individuals used dances to summon assistance from the other world, and drank various magic potions to fall into a mystical, ecstatic trance, a condition that allowed them to become ‘credible’ mediators between, for instance, the Sun God or the Great Manitou and tribe members.

Narcotics and drug abuse is a problem of mankind that goes back thousands of years. Different cultures favoured drugs that can be characterised by one or two dominant types.

Alcohol is typical of Europe. A culture of alcohol consumption evolved and has become established over thousands of years, including related individual and social norms and customs. A passage in the Old Testament (Ecclesiastes 31: 32–36) reads, ‘Wine taken with sobriety is equal life to men: if thou drink it moderately, thou shalt be sober. What is his life, who is diminished with wine? Wine was created from the beginning to make men joyful, and not to make them drunk. Wine drunk with moderation is the joy of the soul and the heart.’ In the New Testament, Jesus turns water into wine, symbolizing the joy and blessing brought to the world, in his first miracle at a wedding in Cana. The most magnificent manifestation of wine as a biblical symbol takes place in the scene when Jesus gives the cup to his disciples over the last supper saying, ‘Drink from it, all of you, for this is my blood of the covenant, which is poured out for many for forgiveness of sins’ (Matthew, 26, 27–28). Thus, wine became a means of redemption and a manifestation of the Eucharist.

As the Prophet Mohammed forbade Muslims to drink wine, a culture of wine drinking could not arise in the Muslim world, instead, the consumption of hashish (cannabis), and the smoking of opium took its place.

In South America, the pre-colonial culture of chewing coca leaves, which contain cocaine, had a function similar to that of alcohol in Europe. These

substances were first used for cultic purposes, or even as medicine. Strong family, tribal, and clan bonds as well as age-old local customs ensured that the use of such substances would be confined to limits within which they posed no threat to health of the population.

With colonialism, further opportunities opened up for many cultures to use drugs that were as yet unknown to them, first as medicines and then as regular consumer goods. The conquerors of South America brought the natives new types of drugs, such as alcohol, or 'firewater', causing a major decline of morals and damage to the local economy. It was again foreigners who introduced opium in China, where opium smoking became so popular that it threatened the work discipline and general living conditions of the inhabitants. Realizing this, the Emperor eventually banned opium smoking. In response, the British sent troops to China, which was defeated in the First Opium War and ceded Hong Kong to the British Crown. The British stopped the most profitable export of opium to China as late as 1919. The drug problem in China, mainly opium, reappeared in the late 1980s. The number of registered drug addicts increased from 70,000 in 1990 to one million by the end of 2002.² Cocaine in turn came into Europe from the Americas after 1492.

The abuse and trafficking of drugs emerged in the second half of the 20th century as a social problem in Western European and overseas countries; in Hungary, this issue has become prominent only over the past decade due to a considerable increase in the number of drug users and dealers. Many states in the Central European region, including Hungary, are no longer transit countries, but have also become destinations for drug trade. Governments and police have made hundreds of reports and implemented numerous programmes in the last few years revealing that an increasing percentage of producers, suppliers, and dealers are young in age. More and more young people are ready to take the risks of being caught and prosecuted in the hope of getting rich quick.

The drug trade is controlled by people involved in organised crime, who often have connections to international criminal organisations. The quantities of drugs – including cocaine, marijuana, and ecstasy – seized in Hungary increased between 1996 and 2002. There was a nearly twenty-fold increase between 1996 and 2003 of ecstasy consumption, while there was a decrease in hashish seizures. Drug consumption patterns were transformed by 2003, seized quantities of marijuana and heroin are again growing, while cocaine is on the decrease. In Hungary, there has been an extremely rapid upsurge in drug abuse offences since 1998. While the number of incidents reported in 1997 was only 943, the figure rose to 4775 in 2002 and then dropped back to 3378 in 2003. All these figures are well below those in Western countries. In New York, for example, 4298 murders were committed in the two years 1990 and 1991 and cocaine was detected in 31% of victims' bodies.

It is worth mentioning that material losses suffered in relation to drug trafficking and consumption are very high in the US and amounted to US\$160 billion in 2000, US\$100 billion of which was due to criminal acts. In the UK approximately 4 million people use at least one illicit drug each year,³ one million use heroin or crack cocaine.

Neurochemical Basis of Happiness. Dopamine – ‘The Happiness Hormone’

The neural network in the brain has approximately 100 billion neurons that communicate with each other by means of chemical substances that are called transmitters. Cognitive and non-cognitive stimuli from the outside world as well as messages received from within the human body and through receptors in the nervous system are processed and stored, and are often linked to previously stored experiences by this huge network of nerves.

Chemical transmitters in the brain, such as glutamic acid and gamma amino-butyric acid (GABA) transfer stimuli from one nerve cell to the other in synaptic connections. However, other transmitters, serotonin, noradrenaline, acetylcholine, and dopamine, which are stored in nerve terminals do not make synaptic, intimate connection with the cell bodies or terminals of other nerve cells,⁴ but are released into the intercellular space (which accounts for 20% of the total volume of the human brain) and able to diffuse away from release sites and carry ‘messages’ through the intercellular space. A neuronal pathway starting from the ventral tegmental area (VTA) of the midbrain running to brain areas responsible for emotions (e.g. nucleus accumbens), intelligence (e.g. cerebral cortex) and decision-making, transmits stimuli using dopamine as transmitter. The latest research has shown that dopamine released in the limbic system, which is the brain area responsible for emotions and emotional reactions, generates a feeling of satisfaction and happiness. This part of the brain may also be called *the happiness centre*, and that is why dopamine has been called ‘the happiness hormone’.

This neuronal pathway operating with dopamine is activated in several situations.

- (1) When one is having a delicious meal, stimuli are transferred via taste receptor cells on the tongue to the VTA, from where, if they are intense enough to excite cells in the VTA, there is a release of dopamine in the limbic system, resulting in a feeling of joy.
- (2) Sensual pleasure, such as sexual excitement, also activates this ‘reward system’, releasing dopamine and causing a feeling of happiness.

- (3) Cognitive stimuli are able to activate this pathway resulting in a feeling of satisfaction.

A function of this mechanism is to generate a desire for eating and reproduction, the former being a basic condition of subsistence, the latter of the preservation of the species. Prolonged physical activities, such as sport or manual labour, increase the synthesis of endorphins in the human brain, which inhibits the release of GABA which in turn increases dopamine release giving a feeling of satisfaction and joy. The endorphins are endogenous peptides having activity exactly like morphine and heroin.

It is not only internal stimuli related to self-subsistence that exert their effects in the limbic system, but also various different scents. My colleagues and I have recently proved that, in response to electrical excitation, or drugs such as ecstasy, dopamine is also released in the olfactory bulb, the brain area where nerve tracts

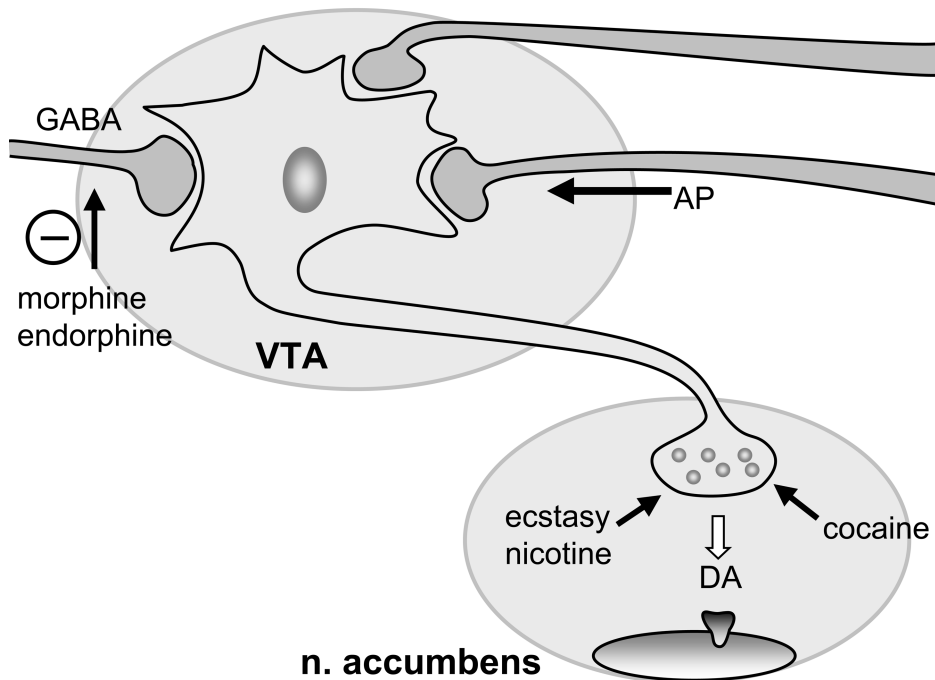


Figure 1. ‘Reward’ pathway (mesolimbic dopaminergic pathway). Drugs of abuse may produce the release of dopamine (i) directly from the varicosities (amphetamines, ecstasy); (ii) inhibiting the uptake of dopamine (cocaine) thereby increasing the concentration of dopamine at receptor sites; or (iii) inhibiting the inhibitory inputs (e.g. the release of GABA, cannabis, endorphin, morphine etc) to the ventral tegmental area (VTA), thereby the release of dopamine is more effective. Note that physiological inputs (cognitive or non-cognitive) to VTA releases dopamine in the limbic system.

from the nasal area (i.e. that of sense of smell) terminate.⁵ This relates to the fact that it is mainly olfactory stimuli that attract male dogs, cats and other animal species to mate. Accordingly, this brain area is proportionately much larger in such animals than in humans. It is well known that desire for the opposite sex is much more complex in humans and is associated with vision, touch, hormonal conditions, as well as a recall of intellectual and emotional memories.

An experiment by Balázs Gulyás and colleagues has shown that the nucleus accumbens, i.e. the emotional and happiness centre, of a Hungarian individual listening to the national anthem of Hungary reacted with an increased activity!

One can summarise the position that in recalling memories associated with pleasant feelings (the sight of a beautiful painting or a landscape or a photograph of a loved one, a stroking by one's beloved, or the smell of a pleasant odour) a repeated excitement of the brain area responsible for emotions, i.e. the happiness centre, causes dopamine to be released in the limbic system and generates a feeling of joy and happiness; the recollection of pleasant memories can elicit, although with a lesser intensity, the feeling of happiness associated with the original experience. The fact that dopamine is needed for this process is confirmed by everyday clinical experience with medicines that act as inhibitors of dopamine receptors, such as phenothiazine-type tranquillisers. These drugs reduce or inhibit reactions related to the feeling of joy, and may lead to emotional desolation.

Most drugs of addiction activate the mesocortico-limbic dopaminergic system to release dopamine in the nucleus accumbens, in the limbic system, in the emotional centre, and in the happiness centre, generating a feeling of satisfaction.⁶ Alternatively, they may release dopamine directly from the nerve terminals of dopaminergic neurons (ecstasy, nicotine, amphetamine), or inhibit the re-uptake of dopamine once released (cocaine) or use inhibitory neurotransmitters to antagonize the activity of GABAergic nerves (morphine, enkephalin, cannabis).

The happiness centre of the brain is responsible for dependence on and addiction to various drugs of abuse.⁶ Addicts feel an irresistible craving for the pleasurable feeling elicited by drugs, and need increasingly large doses to achieve the desired effect.⁷

Drugs as Consumer Goods – On the Waves of Fashion

Opium, Morphine, and Heroin

Opium is the milky latex of the poppy (*Papaver somniferum L.*). The word 'opium' comes from the abbreviation of the Greek term *opos mekonos*, meaning 'the juice of poppy'.

Containing over twenty alkaloids, raw opium is processed differently to suit different types of use. The strongest analgesic alkaloid was isolated and named

morphine after the Greek god of sleep (Morpheus) by Sertürner in 1806. Opium was known already to the Sumerians in ancient antiquity. The first written record of opium use was by Theophrastus, dating back to the third century BC. The *Ebers Papyrus*, dating back to about 1550 BC, shows that the sap of unripe poppy-heads, that is, opium, was used to kill pain in early times. Arabic doctors were also familiar with the use of opium and they introduced it into European medicine.

The use of opium as a medicine in Europe dates back to the 16th century when the German physician Paracelsus (1493–1541) first made use of it. In the 17th and 18th centuries, Laudanum, a mixture of opium and alcohol, was prescribed for colds or headaches. Laudanum was also used to treat tuberculosis sufferers, because it stopped the cough due to its morphine and codeine content.

In Shakespeare's *Romeo and Juliet*, Friar Laurence gives Juliet a glass of potion that will make her sleep and appear as if dead. The plan is that she will awake in the tomb, elope with her lover Romeo and live happily. But, as is usual in tragedies, something unexpected happens. In the morning, her nurse discovers that Juliet is not waking up:

... Why lamb, why lady! Fie, you slug-abed!
 Why love, I say, madam, sweetheart, why bride!
 What, not a word? You take your pennyworths now,
 Sleep for a week; for the next night, I warrant,
 The County Paris hath set up his rest
 That you shall rest but little, God forgive me.
 Marry and amen! – How sound is she asleep!
 ... Alas, Alas! Help, help! My lady's dead! ...

When seeing her daughter's sleeping and seemingly lifeless body, Capulet, Juliet's father, says the following:

Ha, let me see her. Out alas, she's cold!
 Her blood is settled, and her joints are stiff;
 Life and these lips have long been separated

What may Friar Laurence have given to Juliet? Shakespeare, who was familiar with the effects of opium, a drug widely used as a sleeping draught at the time, has the Friar explain as follows:

Then gave I her – so tutored by my art –
 A sleeping potion, which so took effect
 As I intended, for it wrought on her
 The form of death ...

The symptoms are so well described by Shakespeare that it can be established definitively that Friar Laurence gave the girl opium. Across the centuries, some well-known figures such as Pierre de Ronsard and Cardinal Richelieu, as well as

many writers, like Mme. de Staël and Theophile Gautier, would stand against the established social order not only through their literary works, but they would also escape the boredom of everyday life in a state of ‘opium inebriety’. Around 1840 there were estimated to be hundreds of ‘semi-secret’ opium dens (*fumerie*) in France (mostly in Paris and the port towns). Gautier’s example was followed by a number of famous authors, including Baudelaire, Cendrars, Colette, Apollinaire, and Cocteau.

The use of opium as a narcotic drug on the Continent was not as wide ranging as in Britain, where it spread like an epidemic. It was estimated that between 16,000 and 26,000 shops sold opiates in Britain in the 1850s. One London chemist had 378 different opiate preparations on his shelf.⁸ Opium consumption and addiction in America reached its first peak during the years of the Civil War (1861–1865), opium being almost the only medicine for wounded soldiers. The fact that about 4% of the post-war adult population used opiates regularly is mostly attributed to this fact. Opium was used to treat endemic dysentery, and as a preventive against malaria and diarrhoea.

It was only as late as the mid-19th century that the realisation came that people did not only take drugs for reasons of health, but also because of addiction to their psychic effects. As a result, the 1868 Pharmacy Act restricted the sale of opium and opiate products to professional pharmacists in Europe. Before the end of the 19th century, medical products that contained opium and morphine were all declared to be poisons, which made access to them difficult, and the illegal drug trade emerged.

Thomas de Quincey (1785–1859), who became addicted to laudanum, writes in his book entitled *Confessions of an English Opium Eater*:

If opium-eating be a sensual pleasure, and if I am bound to confess that I have indulged in it to an excess, not yet recorded (I say: for there is one celebrated man of the present day, who if all be true which is reported of him, has greatly exceeded me in quantity) of any other man, it is no less true, that I have struggled against this fascinating enthrallments with a religious zeal, and have at length accomplished what I never yet heard attributed to any other man – have untwisted, almost to its final links, the accursed chain which fettered me.

And then he asks, ‘How came any reasonable being to subject himself to such a yoke of misery ...?’

A similar lesson emerges from Baudelaire’s *Artificial Paradises*, a book that gives an insight into the pleasures and terrors of hashish and opium consumption. Baudelaire clearly understood that sensory perception is detached under the influence of opium by hallucinations, from the domination of thoughts and decisions, and that this can lead to an alteration of personality. Paintings by Gustave Klimt and Alphonse Mucha depict this colourful world with orgiastically entwined forms and geometric shapes transformed into wild visions.

Opium smoking was fashionable in the interwar years, but the shock of the Second World War, the post-war struggles for basic survival and the difficulties arising in the procurement of narcotics throughout Europe, led to a nearly complete cessation of the habit. A new epidemic of drug use started in 1964 and is still growing. Illegal opium is usually delivered in the form of small bricks or biscuits to processing facilities. Small bits of opium are either smoked in pipes or drunk dissolved in an alcoholic solution.

The most widely used illegal opiate is heroin (diacetyl morphine), a semi-synthetic morphine derivative.⁸ In fact, heroin is a 'prodrug', from which morphine is produced as an active metabolite in the human body. The use of this drug became widespread in the 1960s, partly due to the relative availability and partly to the population explosion after the Second World War. In the 1960s, raw opium was shipped by the Corsicans from Turkey to Marseilles (the 'French Connection'), where it was converted into heroin that was then transported to America. The number of heroin addicts in the US reached 750,000 by 1970. In 1971, 42% of American soldiers in Vietnam used heroin.

Intravenous use of heroin and morphine is preferred because it results in a high blood level and a subsequent high drug concentration in the brain, immediately causing a general feeling of warmth, and an experience of rapture akin to sexual orgasm, also dubbed as a 'rush', 'kick', or 'thrill'. These are the symptoms that directly lead to abuse. This state of feeling, however, lasts for about 45 minutes only, followed by euphoria, then a sense of deep calmness and sleepiness (the 'nod of the head'). Intoxication is normally caused by variations in the purity of street heroin or the mixing of heroin with alcohol or another central nervous system depressant. The first dose a relapser takes after withdrawal symptoms have passed may be fatal, because tolerance to the drug has by then diminished to a large extent and the usual dose can now lead to a toxic depression of respiration.

Amphetamine and ecstasy

The use of amphetamine and its derivatives is a special area of drug abuse. A survey that American physicians published after the Second World War revealed that there had been a significant increase in cases of psychosis in Luftwaffe pilots who had used amphetamine. At that time, amphetamine, a substance that reduces fatigue and produces alertness, had been used to prolong the flight time for German pilots (and thus to compensate for human losses).

Ecstasy, related in chemical structure to both the stimulant amphetamine and the hallucinogen mescaline, is mostly used by those who attend all-night 'rave' dance parties. It can produce both psychostimulant and psychedelic effects. Ecstasy's pleasurable effects can include an enhanced sense of pleasure and

self-confidence, increased energy, and feelings of peacefulness, and closeness with others. Many disco-goers do not drink alcohol, as amphetamine derivatives are more effective in releasing inhibitions and promoting communication through body language. The normal stimulant effect amphetamines have is also beneficial for typical users, helping them dance all night in a state of permanent and deep ecstasy. The sexually arousing effects of these drugs, combined with a complete loss of inhibitions, often lead to users having frequent sexual intercourse without any protection, and are a source of HIV infection and unwanted pregnancy. The drug effects, including exhaustion, sudden loss of weight, exaggerated heart rate and acute psychosis – including hallucinations – frequently necessitate urgent medical intervention. Ecstasy users need treatment for the after-effects, including depression, anguish, and paranoid symptoms.

Cocaine

Cocaine is an extract of the leaves of the coca shrub that South American Indians chewed long before colonisation. The native people living on the slopes of the Andes knew that the leaves of this plant could improve physical strength as well as reduce hunger and fatigue experienced at high altitudes. The coca shrub was first brought to Europe around 1580. Cocaine, a psychoactive alkaloid, was first extracted from coca leaves in 1860 and was one of the ingredients of an early version of Coca Cola! In 1914, the Harrison Narcotics Act banned the use of cocaine for non-medical purposes in the US.

Today, cocaine is the most common drug of abuse, particularly in Western countries. 1994 statistics published by the National Institute of Drug Addiction show that in the US there were 5 million users and over 20 million had tried cocaine at least once. Relatively inexpensive, cocaine is widely available.

The usual method of use of this substance can, however, produce rapid addiction, psychiatric disorders (anxiety, depression and psychosis), reduced sexual drive and often lead to intoxication or even death. Drug abuse in males occurs twice as frequently as in females. However, smoked cocaine use is particularly common in young women. Nevertheless, there is a gender difference in responses to cocaine. Women consistently rated their overall well-being higher than men after taking cocaine.⁹ The effects of cocaine are related to its inhibitory effect on a dopamine transporter, which leads to an increase of extracellular dopamine concentration in mesolimbic and mesocortical reward pathways of the brain. But it also blocks both noradrenaline and serotonin re-uptake, and thus increases the effect of sympathetic stimulation. It dose-dependently increases heart rate and blood pressure, improves performance on tasks of vigilance and alertness, supports self-confidence and produces well-being. In higher doses it produces euphoria followed by a desire for more drug.

Hallucinogenic substances¹⁰ – mescaline and LSD, the new drugs craze

Native Mexicans used a decoction of the root of a cactus called mescal in their religious rituals. The first full description of the effects of the decoction made from Peyotl (or Peyote) cactus was published in a *De Historia plantarum Novae Hispaniae* by Hernández, personal physician of King Philip II of Spain. The German pharmacologist Ludwig Lewin encountered this cactus during his trip to America and (having named it *Anhalonium lewini*) extracted some alkaloids from it. In his later book, he gave a description of this plant that had such peculiar effects. The Peyote brew until 1890 was only used in North America, and then it spread all over the American continent. Members of the Native American Church made the use of mescaline one of their official religious ceremonies.

An accidental discovery by Albert Hoffman contributed d-lysergic acid diethylamide (LSD; the most remarkable psychotomimetic known to date) and was conducive to the development of psychopharmacology as an independent discipline. Due to its side-effects (suicidal urge, bizarre behaviour, unwanted changes of personality, psychic decompensation, depression, psychopathy, paranoid psychosis, persistent hallucinations), the therapeutic use of LSD was eventually sidelined. At the same time, illegal consumption and trade grew to a frightening extent.

In the 1960s, many years after the horrors of Second World War and the holocaust, European and American nations were beginning to enjoy the benefits of peace and increasing welfare, while young people grew generally discontented and took to the streets in demonstrations, occupying universities out of a desire to be different from their parents. An account of these feelings is given by Salinger in *The Catcher in the Rye*. The hero of this novel is a 16-year-old American high school student, Holden Caulfield, who rebels against the world surrounding him because he thinks love is missing from it.

Influencing unprecedented masses of young people, the music revolution was marked by the enormous success of The Beatles. The title of the famous Beatles song *Yellow Submarine* was an allusion to amphetamine substances, very popular at the time and sold in yellow capsules. This strange world is the subject of the film *Easy Rider* as well as Jack Kerouac's novel *On the Road*. Paintings by Salvador Dali and Victor Vasarely may also be interpreted as depictions of this peculiar, distorted view of life.

The use of hallucinogenic substances was one of the most important manifestations of togetherness, more important than clothing, for the growing hippie movement at the time. Hippies felt most comfortable in the world of strange, colourful hallucinations induced by marijuana and LSD, an atmosphere

reflected in a number of art works intended to reveal the effects of LSD. The many examples include one of the most famous Beatles songs, *Lucy in the Sky with Diamonds*, that is said to reflect the state of mind in which it was written, not only through the initials of the title, but also through the music and lyrics. Lennon and McCartney denied that the song's title was an allusion to LSD, claiming that Lennon's four-year-old son had given this title to a picture he painted while at school. Whatever the truth, they sang openly about drug experiences in another one of their songs, *Help*: 'I'm not so self assured, now I find I've changed my mind and opened up the doors.' It is possible that this line is a reference to Huxley's seminal book *The Doors of Perception* published in 1954. Dealing with the use and effects of mescaline in the introductory chapter, Huxley writes: 'But the man who comes back through the Door in the Wall will never be quite the same as the man who went out.'

Cannabis (Marijuana)

Cannabis is the most commonly abused illegal drug in Europe and in the United States. Five percent of the total population are regular users in some countries.¹ In Britain, about half of all young people (aged 15–29) have tried it at least once and there are some 3 million regular users. The British Medical Association and the United Nations International Narcotics Control Board are against its decriminalisation because it is a serious risk to public health. The 1961 UN convention on Narcotic Drugs provides the framework for governments' drug laws and it requires nations to legislate against banned drugs, this includes cannabis. Public opinion in most European countries supports the decriminalization of marijuana use, but not the drug trafficking. Although there is a controversy about the potential role of marijuana as a 'gateway' drug that leads to use of more dangerous illicit drugs, the UK government reclassified cannabis from Category B (amphetamines, codeine, barbiturates) to Category C (anabolic steroids and benzodiazepines).¹

Abuse of prescription and over-the-counter drugs (pain relievers, tranquilizers, stimulants and sedatives)

According to Nora D. Volkow,¹¹ the director of the National Institute of Drug Abuse (NIDA), the misuse and abuse of prescription medications is a growing public health concern. In the US in 2003, 6.3 million Americans aged 12 and older abused prescription or over-the-counter drugs. In a 2005 survey by the Partnership for a Drug-Free America, 19% of US teenagers reported having taken painkillers or stimulants to get high. Vicodin and Oxycodin are particularly popular. Both

drugs are now more popular among high school seniors than ecstasy and cocaine. The youngsters believe that prescription medicines, even if they are not prescribed by a doctor, are ‘much safer’ to use than illegal drugs.¹²

This terrible disease must be cured

Drugs that induce fake happiness can excite the neuronal circuitry responsible for happiness, but they generally never leave any trace of memory that could later be recalled to generate positive feelings. Consequently, users (addicts) need to take the drug every time they want to have a feeling of pleasure for a very short time. This is the mechanism of addiction, getting users trapped in a vicious circle. Prolonged use of the above-described drugs poses a grave threat to

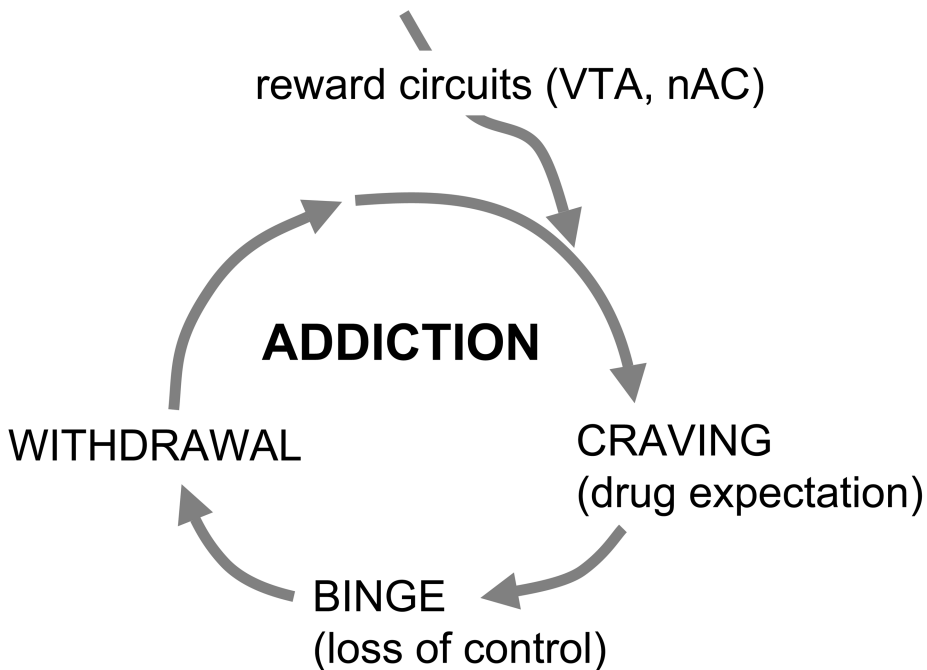


Figure 2. Drug rewards, the vicious circle leading to dependence. Drugs that induce pleasure releases dopamine in the limbic system (‘happiness centre’). The reason to take the drug repeatedly is always related to a reward of some kind (e.g. joy, relief from pain or anxiety). It is now accepted that the condition of dependence that arises from drug abuse is associated with the release of dopamine from the terminals (mainly non-synaptic) of neuronal pathways from the brain stem to nucleus accumbens (mesolimbic pathway). The nucleus accumbens acts as an intermediary between motivation and action.

one's mental integrity, making users develop a psychological and physical dependence, and become incapable of integrating into the family and community, and diverting their physical and mental efforts from studies and work. Drug users have an overwhelming desire and often feel a physical and psychological urge to take drugs again, partly for fear of withdrawal symptoms. They need increasingly large doses, which eventually leads to a permanent mental and physical breakdown.

A man once deeply touched by the world of drugs will no longer be what he used to be. If one has taken a trip to an irrational world for happiness, though it may be a short one, he/she will be a different person, longing for that other world again. Then, a difficult decision will have to be made between the two ways of achieving happiness: the rather harsh real world with human values and the easy, artificial world that is valueless. This is a question that has to be answered by a moral decision.

A political declaration of the United Nations Organisation adopted at a special session on 'countering the world drug problem together' (New York, June 1998) highlights that 'Drugs destroy lives and communities, undermine sustainable human development and generate crime. Drugs affect all sectors of society in all countries; in particular, drug abuse affects the freedom and development of young people, the world's most valuable asset. Drugs are a grave threat to the health and well-being of all mankind, the independence of States, democracy, the stability of nations, the structure of all societies, and the dignity and hope of millions of people and their families.'

What should be done? How can we prevent the situation from escalating and save youth from this awful threat? How can we provide an alternative for young people to help them choose lasting natural happiness derived from the inner self against the 'artificial paradise' that leads to spiritual desolation and bodily deterioration? As Baudelaire writes in *Artificial Paradises*: 'In fact it is forbidden to man, under penalty of intellectual decay and death, to upset the primary conditions of his existence, and to break up the equilibrium of his faculties with the surroundings in which they are destined to operate; in a word, to outrun his destiny, to substitute for it a fatality of a new kind.'

The fight against mass addiction to drugs of abuse requires joint action by national governments and communities. While the state has to use its own specific means and resources primarily to promote prevention, communities bear an even greater responsibility, as the spread of this disease, which, again in the words of Baudelaire, 'Tends to diminish human free will and necessary pain,' must and can be best prevented at the family level. Intellectuals, print and electronic media, and scholars and scientists who are aware of the destructive force of drug addiction on the individual and on society, must also take action, for prevention

is a challenge for all who have a sense of responsibility for their fellow human beings.

References and Notes

1. L. L. Iversen (2004) Cannabis and the law-high time for reform? *European Review*, **12**, 513–525.
2. C. Zhao, Z. Liu, D. Zhao, Y. Liu, J. Liang, Y. Tang, Z. Liu and J. Zheng. (2004) Drug abuse in China. *Ann. N.Y. Acad. Sci.*, **1025**, 439–445.
3. G. McClelland (2006) Caring for problem drug users. *Nursing Times*, **102**, 26–28; C.S.J. Fazey (2003) The commission on narcotic drugs and the United Nations International Drug Control Programme: politics, policies and prospect for change. *International Journal of Drug Policy*, **14**, 155–169.
4. Functional and neurochemical evidence: E. S. Vizi (1984) *Non-synaptic Interaction between Neurons: Modulation of Neurochemical Transmission* (Wiley). E. S. Vizi (2000) Role of high-affinity receptors and membrane transporters in nonsynaptic communication and drug action in the central nervous system. *Pharm. Rev.* **52**, 63–89. Anatomical evidence: cf. L. Descarries, D. Umbriaco (1995) Ultrastructural basis of monoamine and acetylcholine function in CNS. *Seminars in the Neurosciences*, **5**, 309–321.
5. E. S. Vizi (2004) Distinct temperature-dependent dopamine-releasing effect of drugs of abuse in the olfactory bulb. *Neurochem. Int.*, **45**, 63–71. Odour signals are detected at the nasal epithelium, which gives projection to the olfactory bulb.
6. H. Rang, M. M. Dale and J. M. Ritter (1999) *Pharmacology* (Churchill Livingstone, Edinburgh).
7. NIDA (2006) *NIH Principles of Drug Abuse*.
8. D. Clark (2005) Historical perspectives: opium, morphine and opiates. *Drink and Drug News* www.drinkanddrugnews.net 18 April.
9. E. F. McCance-Katz, C. L. Hart, B. Boyarsky, T. Kosten and P. Jatlow (2005) Gender effects following repeated administration of cocaine and alcohol in humans. *Substance Use and Misuse*, **40**, 511–528.
10. D. E. Nichols (2004) Hallucinogens. *Pharmacol. & Therap.*, **1**, 131–181.
11. N. D. Volkow (2004) Confronting the rise in abuse of prescription drugs. *NIDA Notes* **19**(5), 3. Report of NSDUH (2006) Drug abuse continues to decline among adolescents. *NIDA Notes* **20**, 19.
12. *USA Today* (2006) Prescription drugs find in teen culture. *USA Today*, June.

About the Author

E. Sylvester Vizi is the head of Department of Pharmacology in the Institute of Experimental Medicine, Hungarian Academy of Sciences, and President of the

Hungarian Academy of Sciences. His interest covers chemical transmission in the brain. He has pioneered the concept of presynaptic inhibition of transmitter release and that of non-synaptic 'cross-talk' between neurons. He is Editor-in-Chief of *Neurochemistry International* (1998–), Section Editor of *Brain Research Bulletin* (1996–), and an editorial board member of several other journals. He is the member of several European academies, including Academia Europaea.