PSYCHOACTIVE SUBSTANCES: THEIR CONNECTION TO TRANSCENDENT EXPERIENCES AND PSYCHOTIC PHENOMENA

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Abstract
This paper is a literature review with the aim of investigating the relationship between drug use and the occurrence of psychotic disorders/symptoms or transcendental experiences. The purpose of it is to analyze the historical evidence and scientific data that exist regarding the use of drugs in the occurrence of psychosis or transcendent experience. Initially, both the theoretical background of substance use and the most basic drugs in combination with their effect on the human body are analyzed. Cannabis is the substance that is given the greatest basis and is examined as both an epidemiological and social phenomenon, according to its position in modern reality. Subsequently, the concept of psychotic disorders is analyzed, with emphasis on schizophrenia and its symptomatology. One of the central issues of the thesis is the investigation of the relationship between cannabis and psychosis, according to the research data that exist today. In addition, the historical course of drug use from ancient Greece and other civilizations to modern Psychiatry is examined, as well as the concept of so-called entheogenic substances in the context of transcendental experiences. The bibliographic review demonstrates that cannabis use carries an increased risk of psychotic symptomatology, without of course this relationship being unidimensional. The phenomenon must be studied as it is multifactorial, so that effective interventions can ultimately be developed.

Keywords: psychosis, schizophrenia, cannabis, drugs, transcendent experience

INTRODUCTION

A. GENERAL OVERVIEW

It is believed that the term “drug” was proposed by Galen to describe substances that cause numbness or narcosis through the loss of sensation and paralysis of the body. The term was first used by Hippocrates to describe a state of absence of sensation. Nevertheless, the term “drugs” encompasses all substances, even those that do not cause narcosis. Following certain legal changes, the term “drugs” came to refer to substances with the following characteristics: a) they chemically affect brain functions, b) they affect consciousness and psychomotor activity, c) their use is not associated with medical purposes, d) they result in an increasing pattern of use, and e) through continuous use, they cause psychological and physical disorders, while discontinuation following prolonged use/dependence may result in withdrawal syndrome (Βαγιά 2020 σ. 14; Ρέντας, 2018).

Addictions generally “conceal” biological, psychological, or social causes and are associated with basic human needs, which must be fulfilled. Nevertheless, in cases of excessive gratification of these needs, individuals may tend to develop addictive characteristics, as may also occur when such needs remain unmet. Frequent use of a substance may lead to physical

dependence. However, when substance use is discontinued, the so-called withdrawal syndrome may occur, which can become life-threatening for the individual. Physical dependence can be alleviated through the use of the same substance or a similar one. On the other hand, psychological dependence usually occurs following the onset of withdrawal symptoms and refers to a condition in which the user continues to consume substances in order to cope with negative emotions. Users generally do not acknowledge the dependence they are experiencing (Vassiliadou 2008 p. 141-142; Κηπουργού 2020 σ. 21-22; Χαραλαμπίδης, 2003).

Withdrawal syndrome is a set of symptoms that occurs following the abrupt discontinuation of substance use or a substantial reduction in dosage. The most severe symptoms are observed with substances that are eliminated more rapidly from the human body. Symptoms may include insomnia, hyperarousal, anxiety, rapid heart rate, excessive salivation, as well as seizures. All of these symptoms are experienced subjectively and are usually accompanied by a feeling of fear. In cases involving short-acting substances (e.g., heroin), withdrawal symptoms typically appear 8–12 hours after use and subside after 7–10 days. Heroin, in particular, produces the most severe form of dependence. Conversely, in the case of long-acting substances (e.g., methadone), the onset of symptoms may begin 1–3 days later and persist for several weeks. In this case, the symptoms are milder compared with those associated with heroin or morphine (Κοτρώτσου & Παπαθανασίου 2000; Κηπουργού 2020 σ. 23; Βαρβαρήγος κ.ά. 2014; OKANA, 2020).

B. **RECREATIONAL USE AND YOUTH**

In Western societies, cannabis is commonly associated with drug culture, while public perceptions regarding its use remain diverse and, at times, contradictory. Public opinion tends to adopt a rather one-dimensional perspective on cannabis and its use. Historically, cannabis use has been subject to various forms of prohibition; however, in recent years, the medicinal use of cannabis has been decriminalized in an increasing number of countries. In Greece, in 2019, legislation was enacted permitting the cultivation, importation, and possession of medicinal cannabis, following scientific evidence supporting its use in patients suffering from chronic pain, incurable diseases, and multiple sclerosis. This development contributed to a broader destigmatization of cannabis use, including its recreational use. Consequently, cannabis became increasingly widespread among young people and, in combination with alcohol consumption, was associated with adverse effects on their psychological functioning (Γιαννίδου & Πουλόπουλος 2016; Οικονόμου 2022, σ. 23; Αποστόλου, 2018; Τζεφεράκος & Στυλιανίδης 2019).

With regard to the recreational use of cannabis in the Netherlands, the country introduced establishments known as coffee-shops, which operate under municipal licensing and allow individuals to consume cannabis on the premises. According, however, to international data, their number declined to 614 in 2013, compared with 846 in 1999 (Βαγιά, 2020, σ. 41).

An individual's involvement with psychoactive substances is a complex phenomenon associated with a range of factors. Risk factors associated with substance use include the availability of substances, association with substance-using peers, social exclusion, a problematic family environment, parental substance use, neglect, stress, and a lack of boundaries. Conversely, protective factors include the individual's personal and social skills (e.g., self-esteem, self-control, communication, and responsibility), the presence of personal goals and a vision for the future, stable family relationships, and limited accessibility to substances (Καταγής 2017; ΚΕΘΕΑ, 2018).

Young people may begin experimenting with substance use at a very early age. The substances most commonly used include alcohol and tobacco, whereas less commonly used substances include ecstasy and sedatives. Research indicates that young people who place greater trust in their friends than in their parents are more likely to become smokers at some point in their lives. Compared with girls, boys are more likely to consume alcohol and to engage in risky behaviors. Furthermore, according to young people themselves, alcohol and tobacco consumption may facilitate subsequent cannabis use. Therefore, substance use during adolescence may increase the risk of continued substance use into adulthood (Κοκκέβη κ.ά., 2010).

Young people generally tend to experience a desire and curiosity to explore what is unfamiliar to them. As they mature, they gradually learn to position themselves within their social environment and to identify their needs and desires. This process contributes to the development of their social identity. At the same time, however, adolescence is characterized by certain risks that may increase young people's vulnerability to substance use. During adolescence, the brain undergoes significant processes of maturation. Consequently, substance use during this developmental period may interfere with brain development and affect the normal processes of maturation (Ντάλλα κ. ά. 2012; Γιωτάκος 2015).

C. DEFINITIONS

The term "dependence" first emerged in the early nineteenth century in relation to alcohol use and subsequently came to encompass the use of other psychoactive substances. It refers to a cluster of behavioral, cognitive, and physiological phenomena that develop following the repeated use of a substance and are characterized by persistent substance use despite a lack of control and awareness of, or disregard for, its potentially serious consequences (Λιοζίδου 2018; WHO/UNODC/UNAIDS 2004).

Until 1960, the WHO used the terms "drug abuse," "addiction," and "habituation." The term "addiction" was subsequently replaced by "drug dependence," as the latter was considered to provide a more accurate conceptualization of dependence. Similarly, the term "abuse" was replaced by "harmful use" (Οικονόμου 2022; Maddux & Desmond 2000).

For an individual to be considered dependent, they must progress through the following three stages: 1. the use of a substance for gratification; 2. the systematic use of the substance, involving the allocation of time to seeking and obtaining it, as well as associating with individuals who share the same interest, accompanied by conflicts within the individual's social environment; and 3. the loss of control over substance use despite the negative consequences resulting from it (Τσούνης, 2013).

The term "toxicomania" was first introduced by Reghard in 1885. However, the terms "toxicomania" and "toxicomanic" are no longer used in contemporary scientific contexts, as they are considered to contribute to the social marginalization and stigmatization of individuals who use substances. The APA also notes that the term "addiction" has been applied to certain behavioral disorders, including internet addiction, gambling addiction, and sexual addiction (Γεωργάκα, 2007, p. 43; APA, 2013).

D. HISTORICAL OVERVIEW

Substance use is a phenomenon that has been documented across different historical periods and among diverse populations. It is a multifactorial phenomenon influenced by a range of interacting factors, which makes the development of a universal approach to addressing it particularly challenging (Κηπουργού 2020, p. 9).

Cannabis has been present in China since 10,000 BC, while opium was used in Crete as early as 2,000 BC. During the Middle Ages, both substances were also incorporated into religious rituals. Indeed, historically, many psychoactive substances were derived from plants. Since ancient times, humans have used such substances in an attempt to establish communication with the Divine and to acquire the strength necessary to cope with the adversities of life. In this context, substance use served, among other purposes, the pursuit of recreation and the desire for novel experiences (Μαρσέλος 1992; Χαραλαμπίδης 2003).

The expansion of trade and communication with newly encountered regions contributed significantly to the dissemination of psychoactive substances across the world. As their use became increasingly widespread, it was also associated with serious adverse consequences, including illness and mortality resulting from suicide, homicide, and accidents (Κηπουργού 2020, p. 12).

The use of psychoactive substances in religious rituals has also been documented across numerous cultures worldwide. Their medicinal applications are likewise well established, including their use in the treatment of various conditions (e.g., cannabis and alprazolam) and for the management of pain (e.g., opium/morphine). Similarly, coca leaves and caffeine have traditionally been consumed for their stimulating and energy-enhancing effects. Opium was first introduced into the United States during the nineteenth century, and within a few years, its use had become relatively widespread. Codeine, an opium derivative, was first produced in 1831. Initially employed as a treatment for cough and pain, its use subsequently became associated with opium dependence. Morphine was introduced in injectable form in 1856, primarily for pain management, while cocaine was later used as a treatment for dependence on codeine and morphine. Amphetamines were first introduced for therapeutic purposes in 1927, primarily for the treatment of narcolepsy and ADHD. During World War II, amphetamines were used by soldiers to enhance alertness, while following the end of the war, their use was also frequently observed among night-shift workers (Παπαδοπούλου, 2020–2022, pp. 3–4).

1. GENERAL INFORMATION ON SUBSTANCE USE

Etiopathogenetic factors

Substance use disorder is a comorbidity observed among individuals with schizophrenia or other severe mental disorders, with a lifetime prevalence of 48–56%. The prevalence is particularly high among young, unmarried men (Mueser et al. 1995; Lehman et al. 1996).

According to Βασιλειάδου (2007, σ. 43), the presence of mental disorders within a family may provide an appropriate background for the development of risk factors associated with substance (mis)use and alcohol consumption. Some scholars also argue that a family's social and economic profile can influence young people's relationship with alcohol and substances (Spooner, 1999).

Studies involving twins and adopted children have further indicated the possible existence of an unidentified hereditary factor in substance misuse. These studies have also suggested impaired endorphin secretion in some individuals who misuse substances (Τσιάντης & Πουλόπουλος, 2006).

Humans have an inherent need to belong and therefore seek acceptance within social groups. This need is particularly pronounced during adolescence, when peers provide social support in three main forms: (**1**) emotional support, related to the recognition of close relationships during adolescence; (**2**) tangible support, involving direct assistance; and (**3**) informational support,

involving the provision of information to young people aimed at improving problematic behaviours (Τσιάντης & Πουλόπουλος 2006; Spooner, 1999).

In some cases, young people may sacrifice their personal desires to gain recognition from their peer group. This may become problematic when it involves substance and alcohol use. Thus, the need to belong may contribute to risky behaviours, with peer influence occurring either consciously or unconsciously and often resulting in imitation. Adolescents, in particular, tend to imitate behaviours exhibited by high-status individuals portrayed in the mass media. This is consistent with social learning theory, according to which young people process behaviours and situations through observation, which may be associated with deviant behaviours. Research conducted between 2011 and 2015 indicated that more than 90% of international purchases on the "dark web" involved the buying and selling of drugs (Τσιμπουκλή 2002; Τσιάντης & Πουλόπουλος 2006; Elliot et al. 2008; ΕΚΠΝΤ 2017).

The mass media generally portray alcohol positively, associating it with positive mood and high status rather than with violence, poor health, and accidents, in contrast to the concerns reported by health professionals. Consequently, prevention programmes aim to discourage young people from using substances and alcohol. Adolescence is also a period of identity formation, during which various factors become involved, including stress, self-esteem, and expectations. Psychological stress is defined as "the psychological state of tension associated with physiological and hormonal changes and caused by psychological conflict, traumatic experience, or other influences that cause distress to the individual" (Χουντουμάδη & Πατεράκη 1997 σ. 685; Τσιμπουκλή 2002).

Empirical research has examined the relationship between stress and drug use from both biological and psychological perspectives. Findings suggest that individuals may use alcohol and substances in an attempt to reduce the psychological distress they experience. However, evidence concerning substance use remains inconclusive, although a reduction in psychological distress appears to occur among individuals predisposed to alcoholism (Τσιμπουκλή, 2002).

Similarly, self-esteem, as a compensatory and regulatory factor, is defined as "the sense of personal worth that an individual has for themselves". It is influenced by the individual's environment from an early age and is closely associated with socialization. Positive self-esteem is associated with better functioning, while it is particularly important for children growing up in "high-risk" families (Χουντουμάδη & Πατεράκη 1997 σ. 123; Τσιμπουκλή, 2002).

More generally, substance use may function as an escape from negative emotions and psychological pain. However, this "escape" may result in emotional instability and impaired perception of reality. Researchers suggest that users may perceive substance use as a means of reducing the psychological distress they experience. Patterns of substance dependence also vary between individuals, as dependence may be associated with personal traumatic experiences, including violence, sexual abuse, or abandonment (Τσιάντης & Πουλόπουλος, 2006).

The hypothesis that substance use functions, for some patients with psychotic disorders, as a form of self-medication for negative symptoms and medication side effects is not sufficiently supported by empirical evidence. Reported reasons for substance use include loneliness, social anxiety, and peer pressure, particularly among younger individuals. The latter, which is relatively common, may make it more difficult for individuals to reduce their substance use, as

substance use is often perceived positively within the peer group (Khantzian 1997; Gleeson & McGorry, 2004, p. 127).

Epidemiological data

According to a study by the European Monitoring Centre for Drugs and Drug Addiction, cannabis is the most commonly used illicit drug in Greece. More specifically, according to 2015 data, 11% of individuals aged 15–64 had used cannabis at least once in their lifetime, 4.5% of those aged 15–34 had used it at least once during the previous year, and 9% of individuals aged 15–16 had already used the substance at least once. Regarding opioid use in Greece, in 2019, 1.8–2.7 per 1,000 inhabitants were estimated to be users, while 9,708 individuals were receiving substitution treatment. Finally, according to 2015 data on cocaine use, 1.3% of individuals aged 15–64 had used it at least once, 0.6% of those aged 15–34 had used it at least once during the previous year, and 1% of those aged 15–16 had already used it once. It is also noteworthy that, in 2021, deaths resulting from acute intoxication or overdose increased, according to the Annual Report of SODN-ΕΜΠ on Drugs in Greece (ΕΚΠΝΤ, 2021).

Although drugs are prohibited, their use has increased in recent years, as have the problems associated with problematic use, including various diseases (e.g. HIV/AIDS and hepatitis B & C), which may further stigmatise users and contribute to their marginalisation. This situation may also lead users to engage in criminal activities, frequently resulting in imprisonment. At the same time, despite being illegal, drug trafficking continues to occur, while its effective control and management remain difficult (Παπαδοπούλου, 2020-2022, σ. 5).

It is also important to note that individuals with substance use disorders constitute a population at increased risk of infection, as they are affected by various clinical, psychological, and psychosocial factors (Lagisetty et al. 2017, Peacock et al. 2017).

According to a study conducted among a sample of 592 university students, the following results were reported: 51.4% reported alcohol consumption; 16.6% reported alcohol and cannabis use; 1.6% reported alcohol and other illicit drug use; 3.7% reported alcohol, marijuana, and other illicit substance use; and 73.3% reported consuming alcohol either alone or in combination with cannabis, hashish, or other illicit substances (Perez et al, 2020).

2. CATEGORIES AND TYPES

Based on the legislative framework, psychoactive substances can be classified as follows: (**a**) legal substances: alcohol and tobacco; (**b**) legal substances requiring prescription: hypnotics, sedatives, benzodiazepines, barbiturates, and opioids; and (**c**) illegal substances: cannabis, cocaine, heroin, amphetamines, among others (Βαγιά 2020 σ. 31).

Addictive substances can also be classified according to their effects into the following categories (National Institute on drug abuse 2003):

1. Central nervous system (CNS) depressants: alcohol, cannabis, and opioids. In general, most substances have depressant effects.
2. CNS stimulants: cocaine, ecstasy, amphetamines, and methamphetamines. The effects of each of these substances vary quantitatively across individuals. Nevertheless, they all increase levels of noradrenaline, serotonin, and dopamine in the body (Κοκκέβη κ.ά. 2008).
3. Hallucinogens: various naturally occurring substances (e.g. psilocybin) and synthetic hallucinogens (e.g. LSD). These substances distort an individual's perception of reality and affect mood and thought processes (Simonsen et al. 2006).

a. DEPRESSANT SUBSTANCES

This category comprises substances derived from opium and its derivatives. The most well-known are heroin, morphine, and codeine. The same category also includes sedative pills and barbiturates. These substances produce feelings of euphoria and relief when the individual experiences pain (Kring et al. 2010, p. 472).

Natural opioids include morphine and codeine, which are derived from the opium poppy and produce intoxication. There are also synthetic opioids, such as methadone and pethidine. Opioids have analgesic and anesthetic effects when administered intravenously. Their use alters the perception of reality and time, produces euphoria, and may affect speech. The most serious complication of opioid overdose is respiratory depression. These substances can cause both psychological and physical dependence. In the case of heroin, psychological dependence can be particularly strong, making withdrawal and recovery difficult. In addition, the use of contaminated or previously used needles increases the risk of transmitting infections such as HIV and hepatitis B and C (Κηπουργού 2020 σ. 14-15; Βαρβαρήγος κ.ά., 2014).

Another category of CNS depressants comprises volatile organic solvents, which are inhaled or "sniffed" and can cause intoxication as they diffuse into the CNS. Examples include glue, gasoline, and ether. Another category consists of synthetic pills, which are commonly used to alleviate anxiety. These substances are highly addictive and may cause instability and aggression when tolerance develops and the individual seeks higher doses (Simonsen et al. 2006; Kring et al. 2010).

Alcohol

The effects of alcohol on an individual's mental state are similar to those of cannabis. According to research conducted among adolescents, 10–20% experience problems related to alcohol use. Alcohol use does not necessarily indicate a future transition to "hard" drug use; rather, excessive alcohol consumption during adolescence is associated with alcohol dependence later in adulthood. Alcohol has significant adverse effects on the human body, particularly affecting the heart, liver, and pancreas. It may also negatively affect various brain regions and functions, including memory and learning, as well as the cerebellum, which is responsible for coordinating bodily movements (Herbert 1994; Kaplan & Sadock's 2013; Τραγουδάρα & Ποταμούλα 2019 σ. 9; Economou et al. 2013).

Intoxication results in the loss of behavioral patterns normally guided by rational judgement. It is accompanied by emotions such as anger, sadness, euphoria, and reduced sexual inhibitions, and is characterized by incoherent speech, impaired coordination, and intrusion into other individuals' personal space. Alcohol consumption may also alter the individual's facial appearance, resulting in facial flushing and reddened eyes (Verhagen et al. 2010; p. 228-229).

Notably, students without religious affiliation report higher levels of alcohol consumption than students belonging to Catholic or Protestant denominations. Protestant students, in turn, demonstrated higher levels of control over alcohol consumption than Catholic students (Patock-Peckham et al. 1998; Verhagen et al. 2010, p. 229).

Heroin

Heroin belongs to the opioid class and is derived from a natural substance obtained from poppy seeds. Once heroin enters the human body, it binds to opioid receptors and primarily affects cells involved in the perception of pain and pleasure, as well as those associated with cardiovascular function, sleep, and respiration. It can therefore induce euphoria while also slowing breathing. Frequent use can alter brain function and lead to dependence. Prescription

opioid medications can produce effects similar to those of heroin. Approximately 80% of American heroin users report having misused prescription opioid medications before using heroin. Heroin is also associated with increased levels of self-confidence and reduced fear (Τραγουδάρα & Ποταμούλα 2019; Nixon et al. 2010; Χαΐδου 2016, σ. 31).

Heroin is available as a white or brown powder and can be administered intravenously or intranasally. Its effects appear rapidly and last approximately four hours. It produces a profound sense of calm and relief, to the extent that the individual may become inactive. During the initial phase of its effects, the individual may become highly sensitive to external stimuli (e.g. light or sound), exhibit a vacant gaze, and experience constriction of the pupils. After approximately nine hours, the individual may begin to seek the next dose. Until it is obtained, a characteristic withdrawal symptomatology may develop, including restlessness, insomnia, involuntary movements, vomiting, and other symptoms. Despite these effects, heroin does not appear to cause immediate physical damage in the same way as substances such as alcohol affect the liver. As the effects of the substance wear off, withdrawal symptoms emerge, and the individual may become highly aggressive in an attempt to obtain the substance (Herbert 1994; Μαρσέλος 1997; Kaplan & Sadock's 2013; Τζεφεράκος 2010, σ. 5).

Heroin can result in death through malnutrition, overdose, or infection resulting from the use of non-sterile syringes. Its use also appears to be increasing globally (Herbert 1994, Μαρσέλος 1997, Kaplan & Sadock's 2013).

Among adolescents in Greece, heroin is also referred to by names such as "Πρέζα", "Ζα", "Ζουζού", "Παραμύθα", "Η", among others (Γεωργομάνου & Κάππα 2019).

Barbiturates

Barbiturates are available in the form of tablets, capsules, and injections. They depress the central nervous system (CNS) and can cause dependence. Their use in combination with alcohol or other substances is particularly dangerous and may result in death. They are legally administered only by prescription and can cause physical dependence, with the possibility of withdrawal symptoms following discontinuation (Κοκκέβη και συν. 2010; Coupey 1997).

Their depressant effects are directly related to dosage: at low doses, they induce sleep. Some barbiturates are used to treat insomnia, as they facilitate sleep onset and increase sleep duration. At higher doses, they may cause impaired consciousness, intoxication, respiratory depression, and impaired coordination of thought and speech. As the dosage increases, CNS depression becomes progressively more severe, leading to anaesthesia, coma, and ultimately death (Raymond 2022; Suddock & Cain 2023).

Following awakening after administration, individuals may experience a hangover ("heavy head") accompanied by a sense of disorientation. Repeated barbiturate use can rapidly lead to both physical and psychological dependence. As a result, individuals may develop a strong desire to use the drug and progressively increase the dosage, which may, in some cases, result in death (Rey 2015; Πόπκο 2023 σ. 20).

Benzodiazepines

Their misuse is currently widespread, with diazepam being among the most commonly used. They are also frequently combined with other CNS depressants, such as alcohol and opioids. This combination may cause respiratory depression, which can be fatal. However, determining

a specific benzodiazepine dosage associated with respiratory depression is difficult, as other factors, such as age and body weight, also play a role (Schmitz 2016; Kang et al. 2023).

Inhaled substances and GHB-Rohypnol-Ketamine

The substances most commonly inhaled are primarily hydrocarbons used in industrial applications. They are found in various products used in everyday life, including glue, gasoline, correction fluids, and others. Their use is generally more common among adolescents (Μαρσέλος 1997, Kaplan & Sadock's 2013).

The remaining substances are available in pill form and are odourless and colourless, making their detection difficult. They are frequently administered in cases of sexual assault and are therefore also referred to as "date rape drugs". In 1996, legislation was enacted concerning the punishment for their administration. Adolescents commonly refer to ketamine and Rohypnol by names such as "Roufie", "Rope", "K", and "vitamin K" (Kaplan & Sadock's 2013; Γεωργομάνου & Κάππα 2019).

b. STIMULANT SUBSTANCES

Stimulant substances include cocaine, ecstasy, crack cocaine, and amphetamines (Χαΐδου, 2016).

Cocaine

Cocaine is a psychoactive substance derived from the coca plant that stimulates the central nervous system (CNS). Its refined form, crack cocaine, is frequently used among individuals aged 18–25 years. Both substances can be administered by smoking, intravenous injection, or inhalation. Their misuse may cause psychosis, paranoia, erratic and violent behaviour, mydriasis, insomnia, ideation, respiratory disturbances, seizures, and cardiac arrhythmias. Cocaine use induces euphoria and may remain detectable in the body for 3–4 days after cessation. Following use, individuals may experience marked depressive symptoms, as the pronounced stimulation is followed by reduced dopamine levels, resulting in fatigue and dysphoria. This may reinforce repeated use to reproduce the stimulant effects. Both cocaine and crack cocaine can cause dependence, while their use may also result in respiratory failure or myocardial infarction, potentially leading to death (Κηπουργού 2020 σ. 6; Sin & Norman 2013; Kring et al 2010 p. 481; Simonsen et al. 2006; Τσίντου 2010; Herbert 1994; Μαρσέλος 1997; Kaplan & Sadock's 2013; Raymond 2022, Roque et al. 2022).

Among adolescents in Greece, cocaine is also referred to by the slang terms "Αναψυκτικό", "Κοκό", "Κόκα", and "Χιόνι" (Γεωργομάνου & Κάππα, 2019).

Methamphetamine and MDMA

Another stimulant is ecstasy, namely methylenedioxymethamphetamine (MDMA/MDA), an amphetamine derivative typically administered orally as coloured tablets or capsules. It induces relaxation and increased energy while enhancing feelings of intimacy with others. The term "Molly" refers to the purportedly "pure" crystalline powder form of ecstasy. MDMA can distort the perception of distance and time, induce hallucinations and visual disturbances, and is associated with changes in personality and behaviour, potentially due to irreversible neuronal loss. Its use has also been linked to sudden deaths caused by hyperthermia. Like other stimulants, ecstasy produces intense euphoria and heightened insight, but may also cause anxiety, confusion, dry mouth, and nausea (Μαρσέλος 1992; Χαραλαμπίδης 2003; Αντωνόπουλος & Παπανικολάου 2013 σ. 782; Rofail et al. 2009; Kaplan & Sadock's 2013).

Among young people in Greece, MDMA is also known by the slang terms "Κουμπιά", "Μαντάμ", "XTC", and "Λευκά περιστέρια" (Γεωργομάνου & Κάππα, 2019).

Amphetamine is another CNS stimulant that can be administered through multiple routes. Methamphetamine shares several characteristics with amphetamine and commonly occurs in a crystalline or "ice" form. Amphetamine, a synthetic substance first developed in 1887, is frequently used to reduce fatigue by increasing heart rate and constricting blood vessels. Chronic amphetamine use may produce schizophrenia-like symptoms, hallucinations, and persecutory ideation. More generally, amphetamines induce euphoria and increase alertness, energy, and aggression, with symptom severity increasing with dosage. Chronic use may subsequently result in apathy and depression, while dependence can develop rapidly. As tolerance develops, users may require higher doses, eventually experiencing insomnia and anorexia, which can severely exhaust the body (Κηπουργού 2020; Χαϊδου 2016; Simonsen et al. 2006; Οικονόμου 2022, σ. 16).

Methamphetamine is a stimulant that produces euphoria and increased energy but can cause serious harm, including seizures and severe cardiovascular complications. Neuroimaging studies demonstrate alterations associated with regular use, particularly in dopaminergic systems, as well as in brain regions involved in learning, movement, and memory. Methamphetamine users may consequently experience significant emotional and cognitive impairments (Economou και συν. 2013).

Nicotine

Nicotine is derived from the leaves of *Nicotiana tabacum*. Although initially cultivated in England and Spain, it spread worldwide through trade. Since the 1950s, nicotine has been recognized as an addictive substance with stimulant effects, including tachycardia. Its use is associated with bronchitis, emphysema, coronary heart disease, lung and bladder cancer, and chronic obstructive pulmonary disease (COPD), contributing to the development of anti-smoking campaigns worldwide. Smoking during adolescence is also associated with a greater likelihood of subsequent drug use compared with non-smoking peers. Nicotine is primarily found in cigarettes, various tobacco products, and electronic cigarettes, and its use increases blood pressure and heart rate. These health risks apply to all tobacco products, including hookah tobacco (Μαρσέλος 1997; Λιοζίδου 2014; Kaplan & Sadock's 2013; Economou et al. 2013).

c. HALLUCINOGENIC SUBSTANCES

General overview

Hallucinogens are broadly classified into natural substances, such as mescaline, psilocybin, and so-called "magic mushrooms," and synthetic substances, primarily LSD. Mescaline can also be produced synthetically. These substances have traditionally been associated with enhanced access to the unconscious and the activation of an altered sensory system, whereby users may, for example, "see" sounds or "hear" colours. Users frequently report altered perceptions of space and time, often accompanied by intense anxiety and fear of losing control or reason. Their effects are highly subjective. Although hallucinogens rarely cause dependence, their use may induce psychotic reactions in some individuals. Despite their widespread use, no clear association has been established between hallucinogen use and violence; rather, these substances may reduce aggression and behavioural activation (Τσίντου 2010; Χαραλαμπίδης 2003; Kring et al. 2010 p. 483; Λειβαδίτης 1994 σ. 368; Τζεφεράκος 2010 σ. 5).

Cannabis

Cannabis is the second most widely used illicit drug worldwide after alcohol and is currently considered a mild hallucinogen. Short-term use may cause anxiety, panic attacks, tachycardia, impaired memory and learning, and altered perception, while systematic use may produce toxic effects. At high doses, users may experience altered time perception, intensified sensations, hallucinations, followed by lethargy and deep sleep. Although some users experience euphoria, others develop anxiety or panic attacks. Cannabis is also reported to be the most commonly preferred illicit drug among lower and upper secondary school students (Herbert 1994, Μαρσέλος 1997, Kaplan & Sadock's 2013).

Two well-known psychoactive products derived from cannabis are hashish and marijuana, which are typically smoked alone or mixed with another substance, such as nicotine, and may occasionally be consumed in chewed form. Their effects depend on the user's psychological state, route of administration, and dosage. Marijuana contains up to 12% of the active drug, compared with approximately 40% in hashish, and both are widely used in Eastern countries (Οικονόμου 2022; Kring et al. 2010 p. 466; Μπουρλέση & Σαββόπουλου 2016 σ. 12).

The principal chemical compounds in cannabis are cannabinoids, which are concentrated in the plant's flowers and may also be synthetically produced. More than 113 cannabinoids have been investigated and are classified as phytocannabinoids, synthetic cannabinoids, and endocannabinoids. The four most prominent phytocannabinoids are THC, CBD, THCA, and CBDA. THC is primarily responsible for cannabis's psychoactive effects, whereas CBD is associated with its therapeutic properties and does not produce intoxication or dizziness. Cannabis can be cultivated to regulate CBD and THC concentrations; CBD-dominant plants generally do not produce euphoria and are used in pharmaceutical applications, whereas THC-rich plants may cause dizziness and other adverse effects. THC reaches the brain and affects circuits in the prefrontal cortex and striatum, while interacting with dopamine, γ-aminobutyric acid (GABA), and glutamate systems (Devinsky et al. 2014; Wang et al. 2016; Τσεκουρά, 2007).

According to Γεωργομάνου and Κάππα (2019), cannabis is also referred to in youth slang as “Χόρτο”, “Γκρας”, “Μαύρο”, “Φούντα”, “Λιβάδι”, “Γάρο”, and “Ντουμάνι”.

Contemporary research has suggested an association between cannabis use and the onset of schizophrenia, particularly among individuals with a relevant history. THC, the principal psychoactive constituent of cannabis, may induce hallucinations, a core symptom of schizophrenia, potentially worsening the condition when psychotic symptoms are triggered (Kneisl et al. 2009; Οικονόμου 2022 σ. 18).

The 2019 legislation concerning the unrestricted use of medical and pharmaceutical cannabis influenced public perceptions, with some individuals consequently viewing cannabis as harmless to health. This perception, reinforced among some young people by anti-establishment culture, has contributed to the dissemination of cannabis as a substance without significant adverse consequences. Nevertheless, the scientific literature indicates that cannabis use is associated with medium- and long-term health problems that have not yet been fully characterized (Οικονόμου 2022, σ. 19).

LSD

LSD became widely known around 1960 following reports of hallucinations, panic, delirium, and various out-of-body experiences. It may also produce recurrent memories known as

“flashbacks,” during which users re-experience LSD-related experiences while remaining consciously aware that these perceptions are hallucinatory. Flashbacks may have adverse psychological consequences, such as anxiety, and, when prolonged, may potentially cause organic effects, including CNS damage. LSD is administered orally or intranasally, and tolerance may develop following high doses during the first few days of use. Although it does not appear to cause physical dependence, psychological dependence may develop due to the user's desire to reproduce previous experiences, while cessation does not typically produce a withdrawal syndrome. Its psychological effects are commonly described as a “trip”. Overdose may be fatal, while long-term use carries a risk of psychiatric disorders (Herbert 1994; Μαρσέλος 1997; Kaplan & Sadock's 2013; Botvin & Griffin, 2018).

3. USES OF PSYCHOACTIVE SUBSTANCES

Cannabis was initially cultivated for textile production, while hashish became known in Europe through the Crusades. Cannabis has also demonstrated medicinal properties, including applications in advanced AIDS and bronchial asthma, although its effects depend on the route of administration. Its therapeutic use dates back to antiquity, particularly for pain relief (Herbert 1994; Μαρσέλος 1997; Kaplan & Sadock’s 2013; Χαΐδου 2016, σ. 45).

A study of 1,265 children found that increased substance use was associated with reduced educational achievement. Similarly, adolescent users have been reported to exhibit deviant behaviour, contributing to school marginalization and social alienation (Fergusson et al. 2004 p. 78; Lysnkey et al. 2003 p. 102).

Adolescents may consume alcohol to appear stronger and satisfy the desire to engage in prohibited behaviour without facing punishment, with family dynamics also influencing adolescent behaviour (Herbert 1994; Kaplan & Sadock's 2013).

According to Passie et al. (2008), LSD was first chemically synthesized by Albert Hofmann in 1938 and introduced by Sandoz in 1950, initially for experiments aimed at inducing psychosis in healthy individuals. Recreational use emerged in the 1960s and continues today; however, possession remains illegal because of its hallucinogenic effects (Πόπκο, 2023).

Phenobarbital is a long-acting barbiturate introduced therapeutically in 1912 and remains in use as an antiepileptic treatment. Short-acting barbiturates, however, are also used illicitly, sometimes to alleviate the adverse effects of stimulants or other substances (Coupey, 1997).

According to Kang et al. (2023), benzodiazepines (e.g., diazepam) were developed in the 1960s and became a common treatment for anxiety and insomnia, being considered safer than existing alternatives such as barbiturates. Although numerous substances are currently used to treat anxiety, insomnia, and hyperarousal, the effectiveness of benzodiazepines has contributed to their frequent prescription and subsequent misuse (Πόπκο 2023, σ. 23).

4. A BRIEF HISTORY OF ENTHEOGENIC SUBSTANCES AND TRANSCENDENT EXPERIENCES

Cannabis cultivation in the Greek region may date to the 5th century BCE, as referenced by Herodotus. Ancient Greeks cultivated cannabis for materials such as textiles and rope and also recognized its euphoric and therapeutic effects. Theophrastus (4th century BCE) may have known the plant as “δενδρομαλάχη” or “δενδρομολόχα” and described its effects. The ritual use

of the plant was reportedly kept secret, as it was believed that its disclosure would undermine its perceived magical properties (Σκοδριάνου 2022 σ. 13 –14; Charitos et al. 2021).

Earlier Greek scholarship generally maintained that evidence for recreational or ritual cannabis use in ancient Greece was insufficient. This view was based partly on the limited historical references to its psychoactive effects, suggesting either limited euphoric use or little appreciation of its properties. An alternative interpretation is that psychoactive substances were present but culturally taboo and therefore rarely documented. The Eleusinian Mysteries provide a notable example: held twice annually and attracting participants from across Greece, these rites dedicated to Demeter sought spiritual elevation and an experience of immortality. Some researchers argue that participants consumed *kykeon*, a barley- and mint-based drink potentially combined with the parasitic fungus *Ergot* (*Ergot fungus*), thereby acquiring psychoactive properties (Touw 1981; Hillman 2008 σ. 89; Nilsson 1947; Verhagen et al. 2010 p. 228).

According to Sessa (2014, p. 57), anthropological evidence confirms the ancient ritual use of hallucinogens to facilitate psychological healing. Plants and fungi were used to access memories, while ancient shamans combined roles resembling those of physicians, psychotherapists, and priests, establishing therapeutic relationships comparable in some respects to those of contemporary practitioners (Sessa, 2006).

The Chumash, an Indigenous hunter-gatherer group in the Americas, also used hallucinogenic substances in adolescent initiation rituals. Prior to consuming *Datura*, participants followed a specific dietary regimen; the plant contains hallucinogenic compounds (Baker & Phil, 2005, p. 184). Similarly, *Atropa* and *Madragora* were used in medieval European rituals associated with the initiation of witches (Muller et al., 2003).

Between the 1940s and 1970s, the therapeutic potential of psychedelics emerged, challenging psychiatric approaches that had previously relied heavily on psychoanalysis and unstable interventions such as insulin coma therapy and psychosurgery. During the 1950s, interest in new psychotropic substances, including phenothiazines, increased as physicians sought pharmacological approaches to psychiatric treatment. In the early 1950s, British psychiatrist Ronald Sandison visited Albert Hofmann's laboratory and returned to England with 100 vials of Delysid, initiating one of the earliest large-scale psychedelic treatment programmes for psychiatric patients. LSD subsequently became a means of exploring ancient psychedelic practices and stimulated considerable interest in the cross-cultural role of hallucinogens. Although governmental interventions later restricted psychedelic research, the field experienced renewed development approximately four decades later. While early researchers assumed that psychedelics facilitated access to repressed emotions and memories, advances in neuroimaging subsequently provided empirical evidence supporting aspects of these effects (Sessa 2014 p. 57 - 58; Sessa & Sandison 2009; Sessa 2005; Carhart et al. 2012).

Psychedelic substances such as LSD, MDMA, and psilocybin may have therapeutic applications in the management of memories, particularly those associated with traumatic experiences that impair functioning. Their therapeutic relevance has been investigated especially in relation to anxiety disorders, which remain a major focus of contemporary psychiatry (Sessa 2012; Sessa 2014).

Beyond their therapeutic potential, psychedelics have a significant spiritual dimension. Their subjective effects may facilitate experiences associated with awe, love, the sacred, divinity, and forgiveness. Although psychedelic spirituality has attracted interest among recreational users, it has also generated reservations within medicine, raising questions about whether its association

with the counterculture ultimately hindered systematic psychedelic research (Sessa 2014 p. 59; Roberts 2016 p. 27 – 28).

By the mid-1960s, LSD had been prohibited, restricting its use while contributing to the emergence of a broader drug culture. Young people increasingly used LSD and cannabis as forms of protest against authority, and LSD became associated with creativity and influential developments in art, music, cinema, and culinary culture. This countercultural movement generated opposition from authorities, while many physicians distanced themselves from LSD and discontinued psychedelic research, despite earlier evidence of therapeutic benefits. Some shifted their research toward pharmaceutical substances, whereas others turned to MDMA, which remained legal until its prohibition in the 1980s. This prohibition contributed to renewed reactions within the rave culture of the 1990s. Following the withdrawal of medical support, the hippie movement developed its own psychedelic counterculture through free festivals, communal living, political activism, and ideals of freedom. However, increasing consumerism, widespread substance dependence involving amphetamines and heroin, and the expansion of the cocaine trade weakened this movement. In the absence of medical oversight, the psychedelic message lost influence, while physicians increasingly supported contemporary drug-control policies and emphasized the risks of recreational substance use, eventually extending their opposition to the rave movement (Sessa 2008; Sessa 2014 p. 59 - 60; Sessa 2013).

5. DEFINITIONS

Today, the term “psychedelic” is often associated with the drug culture of the 1960s, whereas “mystery” commonly evokes Christian rituals. Despite their apparent distinction, the practices associated with these concepts were historically interconnected. Extensive archaeological research indicates that psychedelics were used in ancient mystery rites, while contemporary studies suggest that controlled psychedelic use may facilitate experiences supporting culturally specific ontological claims (Baker & Phil 2005 p. 179).

Mystery

According to Simpson & Weiner (1989), the *Oxford English Dictionary* defines “mystery” as: (1) the common designation for specific formal rites of the Christian Church; (2) specifically, the Eucharist or Holy Communion; (3) something analogous to a recognized sacrament or possessing a sacred character; (4) a formal pledge, particularly one ratified through ritual; and (5) a pledge under Roman law (Baker & Phil, 2005, p. 180). The term is therefore closely associated with Christian beliefs and practices, particularly the seven sacraments of the Roman Catholic Church. Although the Western Church recognizes these rites as sacraments, it has never provided an official definition of the concept (Irwin 2003, p. 479).

Like other elements of Christianity, the concept of the sacrament has pre-Christian origins and is closely linked to “salvation,” as exemplified by baptism, through which individuals are freed from “original sin” and incorporated into the community of believers (Baker & Phil 2005, p. 180).

During the Roman period, *sacramentum* was used to translate the Greek *musterion*, possibly derived from *muein*, meaning “to close (the mouth)” or “to keep secret.” Both terms were also applied to ancient mystery traditions, including the Eleusinian rites dedicated to Demeter, whose participants reportedly underwent transformative experiences that were kept secret. Comparable traditions existed elsewhere, notably the worship of *soma* in ancient India and Mithra. These mysteries may have involved substances producing profound existential

experiences, leading some researchers to identify them as psychedelic in nature (Jennings 1987; Wasson et al. 1998; Baker & Phil, 2005 p. 180 – 181; Heinrich 2002; Hoffman et al. 2002).

Psychedelic

According to the *Oxford English Dictionary* (Simpson & Weiner, 1989), "psychedelic" is defined as an adjective referring to a drug that produces an expansion of consciousness, as well as anything related to or produced by such a drug or its use. It may also describe sensory experiences resembling those induced by psychedelic drugs, such as vivid colours or moving patterns. As a noun, it refers either to a psychedelic drug or to a person who uses such drugs or adopts a psychedelic lifestyle.

The term "psychedelic" was coined in 1956 by Canadian psychiatrist Humphry Osmond, during his correspondence with English writer Aldous Huxley. After Osmond administered mescaline to Huxley, they sought terminology that could adequately describe its effects. At the time, the effects of mescaline and similar substances, such as LSD, were often interpreted pathologically (e.g., "toxic psychosis"), partly because much of the existing research had involved psychiatric patients. Osmond and Huxley, however, regarded their experiences as non-pathological and argued that mescaline could "unlock" aspects of the mind, facilitating access to unconscious memories, emotions, and ideas. Consequently, such substances increasingly came to be viewed as tools for exploring the human psyche. This distinction from substances such as alcohol and opium was not entirely new: Louis Lewin, regarded as a founder of toxicology, classified mescaline alongside cannabis and other plants whose effects included hallucinations, delirium, and alterations of consciousness (Baker & Phil 2005 p. 181; Lewin 1980 [1927], p. 48).

During the 1950s, the term "hallucinogen" became established following observations of the pronounced effects of LSD and mescaline on visual processing. More recent terminology includes "psychoactive" and "entheogenic." "Psychoactive" broadly refers to any substance that affects mental functioning, whereas "entheogenic," derived from the concepts of "entheos" ("God within") and "genesthai" ("to become"), has an ontological and spiritual connotation. In 2011, the *Oxford English Dictionary* defined entheogens essentially as psychedelics used for spiritual purposes and associated with an experience of the divine within the individual (Baker & Phil 2005 p. 181; Ruck et al. 1979; Roberts & Ellens 2015 p. 10 -11).

German psychiatrist Hanscarl Leuner, a pioneer in the therapeutic use of psychedelics, distinguished between first- and second-order hallucinogens. The former included LSD, mescaline, psilocybin, psilocin, hashish, and related substances capable of producing visual hallucinations, visions, and alterations in spatial and temporal perception without substantial cognitive impairment. The latter included atropine, scopolamine, and other substances with weaker hallucinogenic effects but more pronounced disturbances of consciousness and prolonged memory impairment (Baker & Phil 2005 p. 181; Leuner 1981 p. 33-4).

Researchers studying substances associated with mystical experiences have not reached consensus regarding terminology. "Hallucinogens" remains the most common term because of the intensity of the experiences they produce, although these substances rarely cause true hallucinations in the strict clinical sense. They have also been described as "psychotomimetics," reflecting their purported ability to mimic psychotic states; however, this term is limited because the resemblance is partial rather than complete. "Psychoactive" is more neutral but overly broad, encompassing stimulants such as amphetamines and depressants such as barbiturates (Barber 1970 p. 28; Wullf, 1991 p. 82).

Despite these terminological differences, substance-induced experiences share several characteristics with traditional mystical experiences, including ecstasy, dissolution of personal boundaries, and a strong sense of having encountered an existential truth. Unlike spontaneous religious experiences, however, they are facilitated by psychoactive substances, raising questions regarding the role of passivity and personal control. Nevertheless, some individuals regard such experiences as genuinely transformative. As with religious traditions incorporating psychoactive substances into ritual practices, appropriate precautions, including the presence of a trusted person, may be necessary (Leeming, 2014, p. 1520).

5. EMPIRICAL CORRELATIONAL STUDIES

Drug use has a social dimension, reflecting individuals' need for group affiliation and social differentiation, including within university settings. Although evidence linking this practice directly to religious functions is limited, ethnographic literature documents psychedelic use in initiation rituals that resemble mystery traditions. Importantly, whether a practice constitutes a mystery depends less on the substance itself than on the context of its use. Mysteries are structured ritual practices that foster group identity within an organized religious framework, a relationship extensively examined during the 1960s (Baker & Phil 2005, p. 183 - 185; Sessa 2006b p. 5).

A well-known investigation was conducted by Harvard researcher Walter Pahnke, who studied 20 theology students, administering psilocybin to half and a placebo to the remainder before a Good Friday service. Nine of the ten participants receiving psilocybin subsequently reported what they considered a genuine spiritual experience. Follow-up assessments years later indicated that participants continued to regard the experience as genuinely mystical and as significant to their spiritual lives (Sessa, 2006b p. 5; Doblin R. 1991). Pahnke subsequently identified nine characteristics of mystical experience: (1) unity, experienced internally or externally; (2) transcendence of space and time; (3) intense positive mood, including joy and peace; (4) a sense of sacredness accompanied by awe; (5) perceived objectivity or reality of the experience; (6) paradoxicality; (7) ineffability; (8) transience; and (9) enduring positive behavioural changes, including greater love for others and a renewed appreciation of life's meaning (Wullf, 1991, p. 184).

Whether such experiences are genuinely spiritual remains contested. Western Christian traditions have generally regarded intoxication as incompatible with communion with God, a position exemplified by Oxford professor S. C. Zaehner, who rejected the notion that psychedelic experiences constitute spirituality. Conversely, cultures such as the Bwiti of West Africa, who use *Iboga* in ritual contexts, and Indigenous North American groups using peyote in religious ceremonies, explicitly integrate psychoactive substances into worship (Zaehner, 1972; Sessa, 2006b p. 5).

The broader significance of this debate lies not necessarily in determining whether psychedelic experiences are intrinsically spiritual, but in their apparent similarity to mystical states and what this may reveal about human brain function. This raises questions about how psychoactive substances can produce experiences interpreted as communication with God and whether they contributed historically to the development of spirituality and religious worship. Some researchers have even proposed that the biblical "apple" consumed by Adam and Eve was actually the psychedelic mushroom *Stropharia cubensis*, which reportedly grows in Palestine (Sessa 2006b p. 5 - 6; McKenna 1992).

According to Sessa (2006b, p. 9), psychedelics may also provide a means of investigating phenomena such as parapsychology and near-death experiences (Luke, 2004). Although other

methods of inducing altered states generally involve substantial changes in bodily chemistry and require conditions such as predisposition, appropriate guidance, and acceptance of discomfort, drug-induced intoxication can produce profound altered states without these requirements (Wullf, 1991, p. 82).

A further study at Johns Hopkins University, led by Roland Griffiths and colleagues, involved 36 individuals experiencing a psychedelic drug for the first time. Approximately two-thirds described the experience as the most spiritually significant of their lives, while one-third regarded it as their primary spiritual awakening; relatives and colleagues also reported increased happiness in the following months. Griffiths suggested that psychedelics might have therapeutic potential for addiction and depression, particularly given the spiritual foundations of some addiction-treatment programmes. Participants had no history of mental illness or psychedelic use, received eight hours of preparation, and underwent the sessions under the supervision of two observers. Half received psilocybin, while the remainder received a placebo or amphetamine. Participants receiving psilocybin reported profound feelings of love and tenderness and an intensified focus on the present. However, approximately one-third subsequently experienced intense fear, with some reporting paranoia, leading Griffiths to caution against recreational psychedelic use (Scientific American Mind, 2006).

6. PSYCHOSIS AND ITS FORMS

The term "psychosis" broadly refers to a state in which individuals experience and believe things that are not consistent with external reality and may be perceived only by themselves. Core manifestations include hallucinations and/or delusions. Psychotic disorders are broadly classified into two groups: schizophrenia-spectrum disorders, most notably schizophrenia, and affective psychoses, most notably bipolar disorder. In addition to schizophrenia, the schizophrenia spectrum includes Schizophreniform Disorder, Brief Psychotic Disorder, Delusional Disorder, and Schizoaffective Disorder (DSM-5 2013; Τραγουδάρα 2019 σ. 26; Bentall 2004; Cromby & Harper 2014 Γεωργάκα & Ζήση 2022, σ.21).

The first systematic formulation of these groups was proposed in 1898 by German psychiatrist Emil Kraepelin, who classified severe mental conditions into three major disorders: (a) dementia praecox, (b) manic-depressive illness, and (c) paranoia. Dementia praecox was considered incurable and characterized by hallucinations and delusions; manic-depressive illness involved marked mood fluctuations between depression and mania, with patients considered capable of recovery; and paranoia was associated with disorganized thought and unusual beliefs. In 1911, Swiss psychiatrist Eugen Bleuler renamed dementia praecox "schizophrenia," conceptualizing its core feature as a fragmentation of psychological functions resulting from affective disorganization and influenced by psychoanalytic thought (Read, 2004).

Historically, schizophrenia was conceptualized by Kraepelin (1919) as a persistent cognitive and behavioural deterioration associated with progressive impairment of the patient's health. This view remained influential in clinical practice for decades, alongside the notion that the individual progressively loses the self through identification with the illness. Davidson (1992) similarly described schizophrenia as a lifelong condition. However, according to Zubin et al. (1983), this conceptualization began to change with the introduction of neuroleptic medication and shifts in mental-health policy, particularly the transition from institutional care toward community-based mental-health services (Gleeson & McGorry 2004 p. 63).
Although several large-scale studies have been conducted over the years using different methodologies, they ultimately produced similar findings. Specifically, at least half of the results indicated complete or partial improvement in the health of the patients under

observation. According to Huber et al. (1980, p. 595), patients with schizophrenia have the potential for recovery during their second and third decades of life. It is also worth noting that, in recent years, the biopsychosocial model has been regarded as a fundamental therapeutic approach in several services addressing psychosis (Gleeson & McGorry, 2004, p. 63–64).

Hallucinations are sensory experiences that occur in the absence of an actual external stimulus. For example, an individual may experience an auditory or visual hallucination, believing that they hear or see a familiar person in front of them, even though that person is not actually present. In addition, an individual experiencing psychosis may have delusional thoughts, that is, thoughts or beliefs that are not based on reality. All these experiences can be frightening for the patient and, in some cases, may lead them to become dangerous to themselves or to those around them. The most common symptoms of psychosis include difficulty concentrating, anxiety, suspiciousness, sensory hallucinations, disorganized speech, thought and behavior, depression, catatonia, apathy, and withdrawal from family and friends. The negative symptoms of psychosis mainly include emotional blunting or apathy, social withdrawal, and lack of motivation. These symptoms can sometimes be difficult to distinguish from those of depression. Nevertheless, emotional flattening constitutes a distinct feature in comparison with depressed mood. The basic symptoms essentially involve deficits in areas such as thought and language and are experienced differently by each individual. They are considered to be features that may develop during the early stages of psychosis. According to a German study by Klosterkötter et al. (2001), the follow-up of eight individuals indicated that certain basic symptoms could function as predictors of psychosis. It is also worth mentioning that basic beliefs may include persistent ideas that the individual themselves or the people around them are evil. These beliefs are considered to develop during the early stages of life and may subsequently influence the individual's psychotic experiences (DSM-5, 2013; Gleeson & McGorry, 2004, p. 32, 57).

Psychosis can be classified into several forms, including brief psychotic disorder, substance-related psychosis, and organic psychosis. Brief psychotic disorder may constitute a reaction to a period of extreme personal stress, while the individual may recover within a few days or weeks. Psychosis may also be caused by the use of alcohol or substances such as methamphetamine and cocaine. Hallucinogenic drugs, such as LSD, can cause temporary states with psychotic features. Furthermore, individuals who abuse alcohol or certain other substances may develop psychotic symptoms if they suddenly stop drinking or discontinue their substance use. Finally, organic psychosis may be caused by a head injury or by an illness or infection affecting the brain. Psychosis may also be understood as a disruption of the structures of the "ego," that is, the psychological defense mechanisms, resulting in difficulty distinguishing between the internal and external worlds and consequently leading the individual to experience an extremely distressing state. In this sense, psychosis may be considered a maladaptive way of coping with anxiety in an individual who also presents a certain degree of psychological vulnerability (DSM-5, 2013; Cullberg, 2003).

This condition begins when the individual starts experiencing disturbances in the subjective way in which they perceive an experience. Before the onset of the first psychotic episode, the individual develops idiosyncratic explanations in an attempt to cope with the intense confusion they experience. These explanations constitute a form of regressive thinking that dominates during acute phases. For example, an individual may believe that an evil person or organization is controlling their thoughts. This belief functions as an explanation for the irrational confusion they are experiencing. The individual may project their anxiety onto other people and often perceive them as persecutors. In order to protect themselves from the malicious gaze of others,

for example, they may wear dark sunglasses. As the condition progresses, the individual may develop more intense auditory hallucinations, which may indicate that the separation between thought and reality is becoming increasingly impaired. This pathway is a common route to the development of a first psychotic episode. There are also some less common cases in which the boundaries of the "ego" remain intact until an abrupt collapse occurs. The individual eventually reaches a point at which they are unable to resist and ultimately adopts psychotic explanations as a way of obtaining relief, although this results in a loss of contact with reality (Gleeson & McGorry, 2004, p. 86–87).
According to M. Bleuler (1984), intense psychological conflicts, such as strong adolescent impulses combined with extreme superego pressure, may increase vulnerability during critical developmental stages. Thus, psychological and biological vulnerabilities may interact directly at significant points in an individual's development, potentially accelerating the onset of psychosis. Such interactions appear to increase the risk of developing psychotic disorders (Gleeson & McGorry, 2004, p. 87).

A study of individuals with psychosis found substance misuse to be a common problem, affecting approximately 45% of patients. For some individuals, alcohol and drug misuse preceded hospital admission, while others continued using substances during hospitalization. Substance misuse may have contributed either to the onset or worsening of psychotic symptoms, alongside psychological distress and social difficulties, which were also associated with hospital admission (Gleeson & McGorry, 2004, p. 45).

According to Robinson et al. (1999), relapses are common during the five years following a first psychotic episode. This period can be particularly challenging for young people, who may struggle to accept changes in their lives, including the need for medication. Poor treatment adherence may lead to severe relapses and increase difficulties in continuing treatment. Other consequences may include substance-related deterioration in health and occupational difficulties, further affecting the individual's social life (Gleeson & McGorry, 2004, p. 8).

The impact of psychotic experiences can be substantial, making empathy and emotional support particularly important during the early stages of illness. In primary care, discharge may occur relatively quickly, meaning that access to more specialized care often depends on significant psychosocial deterioration, a suicide attempt, or an acute relapse. Therapists should also devote time to identifying cognitive deficits and adapting treatment accordingly. During the early stages of schizophrenia, discussions may involve hallucinations, transmitters, security services in relation to delusional beliefs, telepathy, and medication. In individuals with recently developed acute schizophrenia, sedation caused by antipsychotic medication may intensify negative symptoms. Therefore, therapists should recognize and support the patient's efforts to participate in treatment. Acute cases can be particularly difficult, often resulting in restrictions on patients' autonomy and limiting their ability to actively engage in treatment (Gleeson & McGorry, 2004, p. 8, 10, 50, 56).

Psychotic experiences can also negatively affect self-esteem and contribute to self-stigma associated with psychiatric hospitalization. Since psychotic disorders commonly emerge during adolescence or early adulthood, they may significantly affect psychological development and identity formation. Consequently, young people's independence, educational plans, and future employment opportunities may also be adversely affected (McGorry et al., 1998; Erikson, 1968; Kessler et al., 1995; Gleeson & McGorry, 2004, p. 65).
According to earlier literature, obesity and other medical conditions, such as cardiovascular disease and diabetes mellitus, occur more frequently among patients with schizophrenia than in the general population (Περιτογιάννης et al., 2018, p. 448).

Hallucinations in individuals with schizophrenia are predominantly auditory (approximately 65%). The most common forms include voices speaking negatively about the individual, voices commenting on their actions, and voices repeating their thoughts. Other types include persecutory hallucinations, which may lead individuals to become suspicious of particular people without an objective basis, believing that they intend to harm them, as well as grandiose delusions involving the belief that the individual possesses exceptional powers or status, such as being a world leader (DSM-5, 2013).

Schizophrenia is a psychopathological syndrome affecting thought, emotion, and behaviour. It is a complex, highly heritable disorder, estimated to have a genetic contribution of approximately 80%, resulting from interactions among multiple genes and environmental factors. The World Health Organization has identified schizophrenia as a major cause of disability and premature mortality worldwide. Evidence also suggests that subtle abnormalities in information processing and neurological functioning may be present from early life, potentially affecting social adaptation as well as academic and occupational functioning (Buchanan & Carpenter, 2005; Tandon et al., 2008; Merikangas & Risch, 2003; Schwab & Wildenauer, 2009; Carpenter et al., 2003).

One of the earliest documented cases historically described in terms resembling schizophrenia was that of James Tilly Matthews, a patient at Bethlem Hospital who exhibited persecutory and thought-insertion or thought-interception delusions, together with auditory hallucinations (Haslam, 1810).

Although schizophrenia has a heterogeneous course, a substantial proportion of individuals experience persistent difficulties. Its prevalence has traditionally been estimated at approximately 1% of the general population (Μπρακατσέλος, 2022, p. 2).

The symptoms of schizophrenia can broadly be divided into three categories:

1. **Positive symptoms**, which are particularly associated with psychotic episodes and include hallucinations, delusions, disorganised thinking and, in some cases, repetitive or disorganised behaviour.
2. **Negative symptoms**, including social withdrawal, anhedonia and reduced motivation.
3. **Cognitive dysfunctions**, involving difficulties with perception, memory, attention and other cognitive processes (Μπρακατσέλος, 2022, p. 2).

During the twentieth century, the German psychiatrist Kurt Schneider contributed significantly to the development of modern conceptualisations of schizophrenia. He identified a number of characteristic symptoms occurring during the disorder, particularly delusions and different forms of hallucinations. His work influenced subsequent classifications of schizophrenia, in which positive symptoms were historically given particular diagnostic importance (Cromby et al., 2013).

Schizophrenia commonly emerges between adolescence and middle adulthood, with onset frequently occurring during the third decade of life. Its development may be either sudden or gradual, with cognitive and negative symptoms often preceding more overt psychotic manifestations. According to DSM-5 criteria, diagnosis requires the persistence of characteristic symptoms over a period of at least six months. Complete remission is relatively uncommon, and schizophrenia frequently co-occurs with other psychiatric conditions, including depression, anxiety disorders and, particularly, substance-use disorders. Life expectancy may also be reduced by a combination of social difficulties, such as unemployment

and poverty, physical health problems and increased suicide risk (McCutcheon et al., 2020; Whiteford et al., 2013).

Finally, Klein (1946) proposed that excessive fragmentation of the ego could contribute to the development of schizophrenia. She associated this fragmentation with the intense projection of elements of the individual's internal world onto external reality, potentially contributing to persecutory experiences and feelings of being threatened or pursued (DeHoff, 2018, p. 94). Studies have reported higher rates of schizophrenia in certain populations and geographical areas, including northern Sweden, Slovenia, Catholic Canadians and Tamils in southern India, while lower rates have been observed among groups such as the Amish/Anabaptist populations in the United States (Verhagen et al., 2010, pp. 254–255).

Substance use, including tobacco and alcohol, as well as suicidal behaviour, is common among individuals with schizophrenia. Approximately 20–50% of patients may attempt suicide, while around 10% ultimately die by suicide. Schizophrenia is estimated to account for a notable proportion of suicides worldwide, and suicide is considered a major cause of premature mortality among people with schizophrenia and other psychotic disorders. Risk is particularly elevated during the early years of illness, when symptoms may be severe and both patients and their families face significant difficulties in adapting to the disorder (Murray et al., 2003; Heilä & Lönnqvist, 2003; Hor & Taylor, 2010; Power et al., 2003; Gleeson & McGorry, 2004, p. 12).

At least half of individuals experiencing a first psychotic episode have reportedly experienced suicidal thoughts, while approximately 25% may have attempted suicide before contacting mental-health services. Only a minority of suicide attempts in schizophrenia appear to be directly associated with auditory hallucinations. Nevertheless, voices commenting on behaviour and auditory hallucinations more generally have been associated with increased suicidality and suicide-attempt risk. Conversely, some symptoms, including somatic delusions, thought disorder and negative symptoms, have been associated with lower suicide risk. Suicidality may therefore increase particularly during the early stages of recovery rather than during the most acute phase of psychosis, when multiple psychological and social factors interact (Nordentoft et al., 2002; Gleeson & McGorry, 2004, p. 176; Heile et al., 1997; Fenton & McGlashan, 1991; Roy, 1982; Power, 1999).

Aggression is also a concern for some individuals with schizophrenia, particularly during the acute phase of illness. However, relatively little research has examined psychological interventions specifically targeting aggression in psychosis. Adolescence and early adulthood, particularly among males, are generally periods associated with higher levels of antisocial behaviour, although research directly examining the relationship between psychosis and offending remains limited (Gleeson & McGorry, 2004, p. 12; Rutter & Smith, 1995).

Another phenomenon is shared psychotic disorder (SDD), in which an individual develops delusional beliefs shared with another person with whom they have a close and dependent relationship, such as a family member, friend, partner or colleague. The condition has traditionally been described as *folie à deux* ("madness for two"), referring to the interpersonal transmission of delusional beliefs between a dominant individual and a more dependent individual. The dominant person commonly has a diagnosis such as schizophrenia, chronic delusional psychosis or a mood disorder with psychotic features, whereas the dependent person may present with psychological or substance-related vulnerabilities, including alcohol use. Social isolation may also contribute to the maintenance of the shared belief system (Μπάρδα, 2022).

Three traditional forms of shared delusional disorder have been described:

1. **Folie imposée:** the dominant individual has an established psychotic disorder and imposes delusional beliefs on a psychologically healthier dependent person. Separation from the dominant individual may lead to remission of the dependent person's delusions.
2. **Folie communiquée:** the dependent individual initially resists the dominant person's delusional beliefs but eventually adopts them. Unlike *folie imposée*, the delusions may persist even after separation from the dominant individual.
3. **Folie simultanée:** two individuals with pre-existing psychotic disorders gradually develop similar or shared delusional beliefs (Μπάρδα, 2022).

When delusional beliefs are shared by an entire group, such as a religious sect, the DSM-5 refers to this phenomenon as mass psychogenic illness. The dominant individual may develop grandiose beliefs and regard their interpretation of reality as uniquely true, without recognising its potential harmful effects on others. Followers may consequently become immersed in an alternative reality characterised by distortions in their beliefs, perceptions and thinking (Μπάρδα, 2022).

Medicine has historically been closely associated with religious phenomena, and schizophrenia has sometimes been interpreted as a "religious" disorder because individuals may experience delusions, imagined worlds and, in some cases, revelatory or apocalyptic visions. On this basis, it has been suggested that shamans and visionaries from other cultures might have been diagnosed with schizophrenia within contemporary Western psychiatry. From a medical perspective, however, such experiences are generally interpreted as manifestations of psychopathology. Conversely, anti-psychiatry perspectives have argued that people diagnosed with mental disorders may instead be challenging conventional notions of reality and culturally shared beliefs. The anti-psychiatry movement, which emerged prominently during the 1960s, questioned whether psychiatric patients necessarily suffered from mental illness and challenged conventional psychiatric interpretations of unusual experiences (Verhagen et al., 2010, p. 215; Crowley, 2006, p. 5).

Individuals with schizophrenia or schizoaffective disorder may appear more preoccupied with religious ideas and behaviours than people with affective disorders. However, mystical experiences should not be equated with the delusional experiences of schizophrenia. Individuals with schizophrenia may become socially isolated and are often reluctant to share their beliefs with others. Their delusional interpretations may therefore function as a personal framework for understanding experiences that cannot be integrated into ordinary shared reality (Dayringer & Oler, 2004, p. 17; Verhagen et al., 2010, p. 215).

Trauma also appears to be an important factor associated with the development of mental disorders, including schizophrenia-spectrum disorders and mood disorders accompanied by psychotic symptoms (Lataster et al., 2011; Steel et al., 2005). Spiritual crises may arise following relatively ordinary experiences, such as romantic rejection, or more severe events, such as the death of a family member. They may also follow experiences that are socially taboo, with such crises potentially being more intense among individuals who occupy less powerful positions within their societies (Hirst, 2005, p. 9; Rojas, 2021, p. 3).

In contrast to contemporary psychiatric interpretations, societies influenced by shamanic beliefs may understand psychotic episodes differently. Rather than viewing psychosis exclusively as an illness, some such traditions interpret it as the beginning of a process of spiritual transformation and development. The psychotic experience may be understood as an encounter with an uncomfortable truth or as an opportunity to express unresolved personal,

familial or community conflicts that cannot be openly articulated because of cultural norms. Within this framework, psychosis may provide a culturally meaningful way of externalising distress, while the individual experiencing it may potentially be recognised as someone undergoing a transformative process rather than being excluded from the community. This perspective has also been connected with psychodynamic theory, according to which intense emotions that cannot be consciously expressed may be repressed and subsequently emerge as psychological difficulties (Rojas, 2021, pp. 1–2).

Kuhn (1963) further suggested, drawing on phenomenological and existential perspectives in psychiatry, that delusional beliefs may reflect an individual's attempt to establish control over their experience of the world. Human experience can be understood as involving both a shared world of common reality and a personal world of imagination, dreams and desires. In ordinary experience, individuals can distinguish between these domains even when moving between them. In delusional states, however, this distinction may become impaired, with the individual's personal reality replacing the shared reality to such an extent that the boundary between the two becomes difficult to maintain. This experience may involve considerable psychological distress, although its intensity may not always be immediately apparent in socially withdrawn or emotionally subdued individuals and may instead emerge through psychological assessment (Verhagen et al., 2010, p. 215).
According to Jaspers (1946), an idea can be considered delusional if it meets three criteria: (**1**) it is held with absolute certainty and cannot be changed; (**2**) it cannot be corrected or modified by evidence; and (**3**) its content is implausible or false. However, delusional ideas do not necessarily constitute false representations of reality (Verhagen et al. 2010, pp. 216–217).

Some spiritual beliefs cannot be empirically disproved and therefore cannot simply be classified as false, regardless of whether the individual holds a psychiatric diagnosis. In other cases, a delusional belief may eventually prove to be true. For example, a delusional jealousy may lead a faithful partner to become unfaithful because of the pressure exerted by the delusional partner. In such a case, the belief remains delusional despite ultimately corresponding to reality. Conversely, genuine beliefs may be incorrectly classified as delusional by mental health professionals because they initially appear implausible. Limited time and resources may prevent clinicians from adequately investigating the validity of patients' beliefs. Moreover, almost all characteristics traditionally associated with delusions can also occur in non-delusional beliefs, including certain religious beliefs (Young 2000; Jones 1999; Maher 1988; Verhagen et al. 2010, p. 217).

Similarly, Kuhn (1962) noted that scientists may accept scientific theories without having access to all the relevant experimental evidence. David (1999) therefore argued that such cases contribute to the difficulty of establishing an universally accepted definition of a "delusional idea" (Verhagen et al. 2010, p. 217).

The difficulty of diagnosis lies partly in the fact that psychotic and religious or mystical experiences may both involve ideas and perceptions that are not directly grounded in material reality. For this reason, the DSM-5, published by the American Psychiatric Association (2013), emphasizes the importance of considering the individual's cultural and religious context when determining whether an experience should be regarded as pathological (DeHoff 2018, p. 5).

Gruhle (1951) suggested that, when it is difficult to distinguish delusional ideas from ordinary beliefs, attention should instead be given to the structure of the individual's thinking during the delusional experience.

A delusional belief, therefore, cannot be judged solely by whether it happens to be true. For example, a man may be completely convinced that his wife is unfaithful and, in fact, she may be. However, if he claims that he knows this because a particular streetlight was extinguished when he passed it, the conclusion may be factually correct while the reasoning underlying it remains delusional. Jaspers (1959) argued that a delusion cannot be fully understood from the outside: even when another person attempts to adopt the delusional individual's perspective, they cannot fully comprehend how the belief acquired such certainty and intensity (Verhagen et al. 2010, pp. 219, 257).

Segal's (1950) *Some Aspects of the Analysis of a Schizophrenic* provided a detailed account of the thought processes of an individual with schizophrenia. She argued that psychosis involves an alteration in the normal process of symbol formation and introduced the concept of "symbolic equation", describing the tendency to confuse a real object with its symbolic representation (Grotstein 1981).

According to Lotterman (1996), individuals with schizophrenia may experience greater difficulties in emotional regulation than neurotic or borderline individuals, particularly in controlling impulses. These impulses may result in threatening or abusive behaviour, disappear through extreme passivity and emotional withdrawal, or be projected onto others. Lotterman also argued that individuals with schizophrenia may experience poorly defined boundaries between the internal and external worlds, making it difficult to distinguish between self and other, or between internal and external experiences. This lack of differentiation may contribute to feelings of helplessness and to the perception that one's life is controlled by others. Conversely, clearly established psychological boundaries allow individuals to distinguish between their emotions, memories and imagination (Vandekar 2019, p. 43; Lotterman 1996).

Psychosis can therefore be understood as a disturbance of thought and perception. Delusion may involve a transformation of the experienced world, which can appear immaterial, unstable or saturated with an unusual sense of meaning. Consequently, reality becomes difficult to distinguish clearly. The individual experiencing psychosis may turn inward toward consciousness itself, experiencing internal phenomena as more immediate or significant than external reality (Humphries 2017, p. 42; Brett 2002; DeHoff 2019, p. 117).

Religious delusions have been documented across different historical periods and cultures. They may involve persistent and intense beliefs that an individual is God, possesses a divine role, or has been cursed by a divine being. In such cases, the perceived alternative reality becomes the individual's primary and seemingly unquestionable reality. Visions are no longer experienced as fantasies but as genuine perceptions of a transcendent world accessible only to the individual. The person may assume a central role within this perceived reality while losing the ability to critically evaluate these experiences. As the thoughts and experiences become increasingly difficult to distance oneself from, they may dominate everyday life and contribute to disorganized thinking and behaviour, ultimately resulting in a loss of contact with the surrounding world (Verhagen et al. 2010, pp. 229, 245–246).
Kingdom et al. (2010) sought to distinguish religious delusions from healthy religious beliefs. They argued that psychotic beliefs are characterized by disordered, idiosyncratic, or inconsistent thinking, sometimes involving neologisms or weak connections between ideas. Their content may involve God or the Devil, often in combination with themes concerning aliens, government agencies, or other external forces. Religious delusions may therefore be understood as strongly held religious beliefs that are inconsistent with established religious doctrine. In some cases, they may also be associated with self-harm when biblical passages are interpreted literally, such as passages referring to cutting off limbs or removing eyes. Kingdom

et al. (2010) described the case of a 33-year-old patient who experienced sleep difficulties, perceived other people as evil "according to the Bible," believed that they were attempting to control him, and considered himself to be the son of God. He also reported seeing angels who approached him and transformed into swans (DeHoff 2018, pp. 104–105).

Chadwick and Birchwood (1994) interviewed 26 individuals diagnosed with psychosis, 25 of whom were receiving neuroleptic medication. All participants reported auditory hallucinations involving some form of harm to themselves or others, often with religious content, such as the voice of God, the Devil, or both. The researchers described these hallucinations as highly idiosyncratic, suggesting that this characteristic may help distinguish healthy religious experiences from religious delusions (DeHoff 2018, p. 105).

Religiosity and spirituality are frequently present among individuals diagnosed with schizophrenia. However, healthcare professionals may lack sufficient understanding of the importance of religion in patients' lives, resulting in these dimensions being overlooked as psychosocial aspects of the illness. Religion may contribute to reductions in symptoms such as anxiety and depression and may also support interpersonal functioning. It has been reported to have a positive effect in approximately 71% of patients and a negative effect in approximately 14%. Nevertheless, religious delusions do not appear to be directly associated with an individual's personal religious faith (Mohr et al. 2006; Rudalevičienė et al. 2008).

According to Clarke (2005), mystical and psychotic experiences may emerge when experiences are not sufficiently filtered through rational thought. Most individuals without psychosis have difficulty moving away from an ordinary rational state of consciousness. By contrast, individuals experiencing psychosis may have a more permeable boundary between these states and, once they enter an altered state of consciousness, may experience difficulty returning to a rational mode of thought (DeHoff 2018, p. 17).

In a study of 424 participants diagnosed with psychosis and experiencing delusions, 87 reported religious delusions, which were primarily based on internal experiences. In addition to auditory hallucinations, disturbances in thought and unusual behaviour were also observed (Iyassu et al. 2014).

Research also suggests that religiosity may contribute to greater engagement with treatment. Among individuals diagnosed with schizophrenia, religious involvement has been associated with improvements in illness outcomes and quality of life, as well as higher levels of hope and perceived meaning in life (Borras et al. 2007).

Although relatively few studies have examined how religious belief influences delusional thinking, the level of religious involvement prior to psychiatric hospitalization has been found to predict the severity of current religious delusions. These delusions, however, are not necessarily directly related to the individual's religious beliefs (Verhagen et al. 2010, p. 230; Petters et al. 1999; Getz et al. 2001).

More broadly, religious belief and psychosis both occur within the general population and are therefore sometimes examined together statistically. This does not imply a causal relationship between them. Rather, an individual who already holds religious beliefs may develop religiously themed delusions if psychosis occurs. The content of such delusions appears to be influenced by the individual's personal concerns and cultural context, rather than being caused by either religious identity or psychosis alone (Verhagen et al. 2010, pp. 261–262).

7. BIOPSYCHOSOCIAL FACTORS

The causes of psychosis are not fully understood, but several factors are believed to contribute to its development. Research suggests the presence of genetic vulnerability, with some disorders, including schizophrenia and bipolar disorder, sharing common genetic factors. Postpartum psychosis, which develops relatively soon after childbirth, may also be associated with hormonal changes and sleep disturbances, although its precise causes remain unclear. Structural and neurochemical changes in the brain have also been observed in individuals experiencing psychosis, with brain imaging studies indicating reduced grey matter in some people with a history of psychosis. Overall, the aetiology of psychosis appears to involve interactions between biological and psychosocial factors. Consequently, treatment should not focus exclusively on the individual but should also consider the family and broader social environment, which can play an important role (Wainwright et al. 2015; Τραγουδάρα & Ποταμούλα 2019, pp. 29–30).

Studies conducted in non-clinical populations have provided evidence concerning psychopathological outcomes associated with substance use, including psychotic episodes (Carhart et al. 2016; Krebs et al. 2013; Nesvag et al. 2015; Rogers et al. 2009).

The administration of pharmaceutical or psychedelic substances in controlled clinical settings appears to be relatively safe, with a low likelihood of serious adverse events. By contrast, their use at parties, festivals, or in private settings is considered less safe and, in the case of illicit substances, may also constitute illegal activity (Danforth et al. 2016; Henrik et al. 2018, p. 180).

Cannabis is among the most commonly used substances by individuals with schizophrenia. Hambrecht and Häfner (1996) reported cannabis use among approximately 88% of individuals who used illicit substances. Cannabis use has also been identified as an important risk factor for psychosis, with even moderate use potentially increasing the likelihood of psychotic symptoms in individuals who are already vulnerable. Studies of individuals with recent-onset schizophrenia or other psychotic disorders have found a strong association between cannabis misuse and relapse or worsening of psychotic symptoms. Stimulants such as cocaine, LSD, and amphetamines have likewise been associated with the recurrence of psychotic symptoms and with social problems, including violence and criminal behaviour (D'Souza et al. 2009; Weil 1970; Linszen et al. 1994; Gleeson & McGorry 2004, pp. 126–127).

The relationship between substance use and relapse is also closely associated with the social disorganisation and stress experienced by the individual, which may, in turn, reduce adherence to medication. Prenatal stress has additionally been identified as a factor that may negatively affect brain development and increase vulnerability to schizophrenia. In particular, the hippocampus appears to be sensitive to elevated levels of cortisol in the body (Gleeson & McGorry 2004, p. 127; Brown et al. 2005).

Research examining psychosis and cognitive functioning has found that patients experiencing a first psychotic episode who had also experienced childhood trauma showed greater cognitive impairments. Using magnetic resonance imaging (MRI), one study examined the relationship between childhood trauma, cognitive functioning, and amygdala and hippocampal volume in 83 individuals experiencing their first psychotic episode (45% diagnosed with schizophrenia and 55% with another psychotic disorder) and 63 healthy participants. The study found that the mean amygdala volume was smaller among patients than among healthy participants, particularly among those who had experienced childhood maltreatment. Childhood trauma was also associated with reduced amygdala volume and poorer cognitive functioning (Aas et al. 2012; Vandekar 2019, p. 22).

Freeman and Fowler (2009) conducted a study of adults and found that severe childhood sexual abuse was associated with an increased risk of persecutory delusions and verbal hallucinations. However, a meta-analysis by Varese et al. (2012) found no evidence that any particular type of childhood trauma was a stronger predictor of psychosis than others (Vandekar 2019, p. 22).

Kelleher et al. (2013) studied 1,112 adolescents aged 13–16 and found that childhood trauma, particularly bullying and physical abuse, was predictive of psychotic experiences. The findings indicated a relationship between the severity of bullying and the likelihood of experiencing psychotic symptoms. Furthermore, when exposure to trauma ceased, psychotic experiences also decreased in frequency, suggesting an association between continued exposure to adversity and the persistence of such experiences (Vandekar 2019, p. 23).

A large population-based study of 17,337 California residents examined the effects of various adverse childhood experiences on the likelihood of hallucinations. Childhood maltreatment was identified as an important factor associated with psychosis, particularly voice-hearing. Moreover, the likelihood of hallucinations increased as the number of different adverse childhood experiences increased (Whitfield et al. 2005).

Similarly, Dvir et al. (2013) found that childhood trauma and adverse experiences were associated with a 2.8-fold increased risk of psychosis, while individuals with psychosis were 2.72 times more likely to have experienced childhood adversity. The authors estimated that, under a causal interpretation of these findings, removing childhood adversity from the population could potentially reduce the prevalence of psychosis by approximately one third (Dvir et al. 2013).

Conus et al. (2010) examined 658 individuals experiencing a first psychotic episode and found that 34% had experienced sexual or physical abuse. These individuals may also have had PTSD and/or substance-use disorders prior to the onset of their first psychotic episode (Vandekar 2019, p. 24).

Arseneault et al. (2011) similarly investigated traumatic experiences and psychotic symptoms among 2,232 twins aged 5–12 years. Children who had experienced abuse or bullying by adults or peers were more likely to develop psychotic symptoms by the age of 12 than those who had not been exposed to such experiences (Vandekar 2019, p. 24).

According to Elpidis (2024), researchers from Stanford University, the University of California, Universidad del Desarrollo, and the University of Oxford examined approximately 900 six-year-old children, some with a history or risk of schizophrenia/psychosis and others without such a history. More than 100 participants had 22q11.2 deletion syndrome, a genetic condition involving the loss of part of one copy of chromosome 22 and associated with an estimated 30% risk of developing psychosis, schizophrenia, or both.

The researchers used machine-learning algorithms and functional magnetic resonance imaging (fMRI) to examine differences in brain activity between individuals with and without psychosis. The study found that participants with 22q11.2 deletion syndrome showed dysfunction in similar brain regions, particularly the anterior insula and ventral striatum. These regions have been associated with hallucinations and delusions in psychosis. The findings suggest a relationship between psychosis and dysfunctional cognitive filtering, particularly within the brain's salience network, which normally identifies stimuli and assigns significance to them. When this system is disrupted, the brain may incorrectly assign importance or attention

to otherwise ordinary stimuli, potentially contributing to hallucinations and delusional beliefs (Elpidis 2024).

Moreover, the risk of developing schizophrenia appears to be associated with exposure to urban environments. Research suggests a dose–response relationship between urbanicity and the likelihood of developing schizophrenia, with higher risks observed in more urbanised areas. This association, however, does not appear to apply to affective psychoses. Several environmental factors may contribute to this relationship, including population density, characteristics of the physical environment, the presence or absence of pets, and infant-care practices. At the same time, evidence suggests that culture can influence the content and expression of psychotic symptoms. In German psychiatry, Zutt introduced the term "pathoplasticity" to describe the culturally sensitive aspects of the manifestation of mental disorders (Σκώκου 2012, p. 8; March et al. 2008; Tandon et al. 2008; Verhagen et al. 2010, p. 229; Zutt, 1963).

9. NEUROTOXIC EFFECTS OF CANNABIS ON THE HUMAN BRAIN

A substantial body of literature has documented potential adverse health effects associated with recreational cannabis use. This is particularly relevant in the context of medical cannabis, as its legalisation involves prescribing the same plant-derived substance, raising concerns about its potential risks (Σκοδριάνου 2022; Volkow et al. 2014).

Cannabis is commonly classified among "soft" drugs and is generally considered less harmful than substances such as heroin and cocaine, as well as legal substances such as alcohol and tobacco. Its effects, however, depend on factors including the type and amount of cannabis used, patterns of use, and previous exposure (Witton 2008; Kelly & Nappe 2021; Lachenmeier & Rehm 2015; Macleod & Hickman 2010; Hall 2015).

The most common acute behavioural effects include euphoria, altered perception of time, drowsiness, anxiety, and, less frequently, paranoia. Fatal overdose from cannabis has not been documented, while acute toxicity appears to be relatively uncommon compared with other psychoactive substances. Nevertheless, heavy use may contribute to respiratory and cognitive problems (Hall & Solowij 1998; Witton 2008; Hall 2015; Corrigan 2008).

Long-term cognitive effects may be particularly relevant when cannabis use begins during adolescence. Adults who initiated use before the age of 17 have been found to exhibit difficulties in executive functioning. Similarly, research involving individuals aged 14–22 who used cannabis up to the age of 22 found greater cognitive deficits at age 27 compared with non-users of the same age (Pope et al. 2003; Brooks et al. 2008).
The American Society of Addiction Medicine (ASAM) argues against smoking as an appropriate route of cannabis administration and supports regulating cannabis-containing products according to pharmaceutical standards, including prescription requirements. It also opposes cannabis legalisation. Similarly, the American Psychiatric Association (APA) notes that there is insufficient evidence to establish cannabis as a treatment for psychiatric disorders and highlights adolescents as a particularly vulnerable population because cannabis use may negatively affect neurodevelopment. Other US medical organisations, including the National Multiple Sclerosis Society (NMSS) and the American Academy of Child and Adolescent Psychiatry (AACAP), have likewise expressed reservations, noting the limited evidence regarding the medical use of cannabis (Βαγιά 2020, σ. 52–53).

Research has identified an association between greater cannabis exposure and the occurrence of psychosis and schizophrenia, although the nature of this relationship has been debated for many

years. As early as the 19th century, the psychiatrist Moreau de Tours conducted experiments involving cannabis with himself, his students, and his patients. Acute psychotic symptoms were subsequently reported, including agitation, paranoid ideation, disorganised thinking, incoherence, dissociative experiences, depersonalisation, and hallucinations. Negrete later described cannabis use as a potential factor associated with vulnerability to psychotic disorders, worsening of psychotic symptoms and schizophrenia relapse, and poorer response to antipsychotic treatment. Similarly, a 1958 study reported psychotic symptoms, including delusions and disordered thinking, among healthy volunteers following the consumption of Indian cannabis. Cannabis-induced toxic psychosis may involve aggression, hallucinations, paranoid ideation, and other symptoms resembling schizophrenia, although these symptoms generally resolve within several weeks after cessation of use (Hall & Degenhardt 2015; Hall 2015; Zammit et al. 2002; Henquet et al. 2004; Verdoux et al. 2002; Castle & Murray 2004, p. 2; Macleod 2007; Βαγιά 2020, σ. 67–68).

An alternative explanation is provided by the self-medication hypothesis, or reverse causality, according to which individuals within the psychotic spectrum, particularly those with schizophrenia, may use cannabis because of its perceived euphoric effects or in an attempt to alleviate aspects of their symptoms (Βαγιά 2020, σ. 68).

10. NEUROBIOLOGICAL AND CLINICAL FINDINGS ON THE CANNABIS-PSYCHOSIS RELATIONSHIP

Cannabis is one of the most widely used illicit psychoactive substances and contains more than 400 chemical compounds. Among these, Δ-9-tetrahydrocannabinol (THC) is primarily responsible for its psychoactive effects. Cannabis use has been associated with an increased risk of psychiatric disorders, including schizophrenia (Γεωργίου 2011; Kneisl et al. 2009).

Clinicians consistently recognise the potential impact of cannabis and alcohol use on the course of psychosis following a recent diagnosis. Focus-group findings also indicate that patients and their families perceive a complex relationship between substance use, particularly cannabis, and relapse (Gleeson & McGorry 2004, p. 127).

Hambrecht and Häfner conducted a study in Germany examining the relationship between substance use and the early clinical manifestations of schizophrenia. The study included 232 interviews with individuals with schizophrenia and divided those with substance misuse into three groups: those whose substance misuse preceded schizophrenia by more than five years (27.5%), those whose substance use and initial symptoms emerged simultaneously (34.6%), and those who began using substances after the onset of schizophrenic symptoms (37.9%). Approximately 90% had used cannabis at some point, while 14.2% experienced their first schizophrenic episode after a history of substance misuse. Comparisons between individuals with and without such a history revealed no significant differences in the mean age of symptom onset. Male sex, unemployment, alcohol misuse, and younger age at schizophrenia onset were associated with the development of substance misuse (Hambrecht & Häfner 2000; Γεωργίου 2011).

Similarly, a 2002 Dutch study of 133 patients examined the onset of schizophrenia symptoms. Approximately 55% of participants with initial negative symptoms had already experienced them before seeking medical attention. The mean age of symptom onset differed between men (26.5 years) and women (41.6 years). A substantial difference was also observed between cannabis users and non-users: the mean age of onset of initial negative symptoms was 23.7 years among users compared with 38.4 years among non-users. These findings suggest an association between cannabis use and an earlier onset of schizophrenia (Veen et al. 2004).

A 2005 Danish study examined whether psychotic disorders associated with cannabis use subsequently developed into persistent psychotic conditions. Among 535 patients, 44.5% (238 individuals) were diagnosed with psychotic symptoms that subsequently developed into schizophrenia-spectrum disorders, while 77.2% experienced psychotic episodes following admission, with substance-induced and other transient psychotic conditions also observed. Men had a higher risk of developing schizophrenia than women (47.6% vs. 29.8%). Subsequent diagnoses most commonly included paranoid schizophrenia, followed by acute or transient psychotic disorders, personality disorders, and unspecified schizophrenia. Among the 238 individuals with psychotic symptoms, 58% received treatment for paranoid schizophrenia and 20.2% for unspecified schizophrenia. Both male and female cannabis users received their first schizophrenia diagnosis at a younger age, whereas no significant age difference was observed among those who developed schizotypal or schizoaffective disorders (Arendt et al. 2005).

In the same year, Grech et al. (2005) investigated whether cannabis use was associated with more severe positive symptoms among individuals experiencing psychosis. The study initially included 119 patients in Malta, of whom 98 were available for analysis. Their mean age at admission was 25.4 years. Using DSM-IV criteria, 97 participants were diagnosed with schizophrenia (41), affective psychosis (25), schizoaffective disorder (9), delusional disorder (9), atypical psychosis (7), or schizophreniform disorder (6). Of the 98 participants, 61 had no history of cannabis use during follow-up, 9 were using cannabis at admission, 12 began using it during follow-up, and 16 had used cannabis both at admission and subsequently (Grech et al. 2005).

A subsequent North American study conducted between 2000 and 2005 examined the relationship between cannabis misuse and psychosis in 48 participants aged 12–30 years. Participants were divided into groups according to the presence or absence of cannabis abuse based on DSM-IV criteria. Although no substantial differences were observed at the initial assessment, males appeared more likely than females to develop psychosis. During the one-year follow-up, six participants developed psychosis: three met criteria for schizophrenia, two for schizoaffective disorder, and one for bipolar disorder. Nicotine use was also notable, as four of the six participants who developed psychosis used both nicotine and cannabis. No clear association was found between alcohol or cocaine dependence and psychosis. However, the small sample limited conclusions regarding whether age or sex predicted the onset of psychosis (Kristensen & Cadenhead 2007; Γεωργίου 2011).

Interestingly, some studies have reported that individuals with psychosis who also use substances may experience shorter hospitalizations and better functional outcomes than non-users. Several explanations have been proposed. First, substance users may have had better premorbid functioning, reflected partly in their ability to engage in substance use. Second, they may experience a more acute onset of psychosis and a rapid decline in functioning, prompting earlier contact with mental-health services. Consequently, a shorter duration of untreated psychosis may contribute to a better treatment response. Finally, because substance misuse can intensify psychotic symptoms, short hospitalizations accompanied by reduced substance use may lead to subsequent improvement (Andreasson et al. 1989; Arndt et al. 1992; Gleeson & McGorry 2004, p. 139; Norman & Malla 2001; Ries et al. 2000).
Regarding the association between cannabis use and relapse, there is a general consensus at the clinical level. Nevertheless, relatively few empirical studies have investigated this association among patients experiencing a first psychotic episode. An exception is the study conducted by Linszen, Dingemans, and Lenior (1994). In this study, cannabis use was classified into two categories according to frequency: mild use, defined as use ranging from once per week to once

per day, and heavy use, defined as the consumption of more than one cannabis cigarette per day. Of the 93 patients included in the study, 26% were found to misuse cannabis, and 54% of these individuals were classified as heavy users. With the exception of one participant, all participants had initiated cannabis use prior to the onset of psychosis. Regarding relapse, 61% of individuals who misused cannabis experienced a relapse, compared with 18% of those who did not misuse cannabis. Furthermore, an increased risk of relapse was observed among individuals with a history of long-term cannabis use (Gleeson & McGorry, 2004, p. 163)

DISCUSSION

The literature reviewed raises a number of concerns, primarily related to the recreational use of these substances. Although the substances in question appear to possess a therapeutic dimension, they remain an area that has not yet been sufficiently studied. Further research is therefore required to ensure that the scientific community acquires sufficient knowledge, thereby enabling the regulation of their recreational or therapeutic use and, potentially, the relevant legislation itself.

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