Psychiatr. Pol. 2023; 57(3): 657–670
PL ISSN 0033-2674 (PRINT), ISSN 2391-5854 (ONLINE)
www.psychiatriapolska.pl
DOI: https://doi.org/10.12740/PP/150053

Classical psychedelics in psychiatry – renaissance of interest and therapeutic perspectives

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Summary

Substances that change the states of consciousness have been used in the therapeutics of traditional cultures for hundreds of years. In the Western cultural circle, scientific curiosity and hope for a breakthrough in the treatment of various mental disorders constituted the basis of the first wave of research on humans with the use of psychedelics. After synthesizing LSD, psychedelic substances aroused intense but short-term interest among mental health specialists at the beginning of the second half of the 20th century. In the preliminary studies, substances such as psilocybin or LSD, used as a supplement to psychotherapy, showed promising therapeutic effects, however, due to legal and political reasons, all research work was stopped in the 1970s. The last two decades have been a period of renaissance in the interest in using psychedelic substances in psychiatry. Despite the early stage of work, the clinical research conducted so far has indicated the potential benefits of using psychedelics in the treatment of anxiety, affective disorders, or addictions. Moreover, so far, no serious side effects of this form of therapy have been reported. However, due to a number of barriers of both medical and legal nature, the creation of the first psychiatric drug with psychedelic properties appears to be extremely complicated. Further, precisely constructed studies on large groups of patients are needed to determine whether psychedelics can find practical applications in psychiatric therapy (or even become a long-awaited breakthrough in the treatment of mental disorders).

Key words: psychedelics, pharmacotheraphy

Introduction

Terminology

We use the term "psychedelics" to define a group of "soul manifesting" (from Greek: *psyche* – soul, *delos* – manifest, reveal) psychoactive substances that cause changes in perception, consciousness, way of thinking, and feeling emotions. This name was first used by the English psychiatrist Humphry Osmond in his correspond-

ence with Aldous Huxley – in response to the writer's suggestion that LSD, mescaline and similar substances be referred to as "phanerothyme" [1]. The substances in this group are often also called "hallucinogens" – this term does not fully give the effect of these substances since the perception changes occurring after taking psychedelics cannot be called exclusively hallucinations. In order to qualify a given substance as psychedelic, its effects must correspond to a specific characteristic: the dominance of changes in perception, thinking and mood; absent or minimal memory or cognitive impairment; lack of stupor, loss of consciousness, or excessive arousal; slight severity of side effects from the autonomic nervous system; no addictive effect [2]. These criteria are met by a number of substances, including those that cause actions which are different from the purely psychedelic ones. These include MDMA (3,4-methylenedioxymethamphetamine), dexomethorphan, salvinorin A (contained in sage of the diviners) or ibogaine. However, for the purposes of this review, the term "psychedelic" will be narrowed down to the "classic" representatives of this group, mainly affecting the 5-HT_{2A} receptor: LSD (lysergic acid diethylamide), psilocybin (4-phosphoryloxy-N,N-dimethyltryptamine), and DMT (N,N-dimethyltryptamine), and the "classic psychedelics" will be analyzed for their potential usefulness in psychiatric treatment. It results both from the quantity and quality of research available at this stage as well as the similar psychopharmacological properties of the said compounds.

Psychedelics in history

Substances changing states of consciousness have accompanied mankind for hundreds of years. In diverse cultural circles, they were used for healing, religious and ceremonial purposes. The earliest direct evidence for the use of psychedelic property substances comes from 5,700 years ago, from the north-eastern part of Mexico (kidney beans with the addition of peyote, a cactus containing mescaline) [3]. The use of an unspecified psychedelic was probably also the essence of the Eleusinian Mysteries in Ancient Greece [4]. Hallucinogenic mushrooms containing psilocybin grow all over the world, and their consumption for narcotic purposes in the history of mankind seems equally common [5]. Nowadays, mescaline is used, i.a., in the ceremonies of the Native American Church, and Ayahuasca (a drink containing N,N-dimethyltryptamine (DMT) and beta-carboline derivatives that inhibit the activity of peripheral monoamine oxidase type A (MAO-A)) is used during ritual healing and spiritual practices in the region of the Amazon River basin [6, 7].

The first documented contact of modern Western civilization with psychedelics took place in 1897, when Arthur Heffter isolated mescaline from peyote. However, it was the synthesis in 1938, by Albert Hofmann, of lysergic acid diethylamide, more commonly known as LSD, should be regarded as the true beginning of the complicated relationship of Western culture and science with psychedelic substances. Working for Sandoz company's Swiss laboratory, Hofmann was a member of a team studying

ergot fungi derivatives for their potential applications in medicine. LSD, being one of many compounds he obtained, did not raise much attention of the researchers, at first. In animal studies, it showed no specific properties, therefore further work on the substance was suspended. Nevertheless, in 1943, Hoffman re-synthesized LSD, guided by a "peculiar feeling" that the action of this substance goes far beyond the observations made so far. Soon after, the researcher found out about it personally, first after accidental and then intentional taking of the substance. After demonstrating the safe pharmacological profile of the substance, LSD entered the market in 1947 under the name "Delysid." In 1958, Albert Hofmann isolated psilocybin from the hallucinogenic mushrooms, which Sandoz introduced for sale under the name of "Indocybin." Support of the psychotherapy process and the use in experimental studies on the pathogenesis of psychoses were considered indications for the use of both medications [8].

Psychedelic substances in psychiatry

The beginning of the 20th century, the moment of discovery of mescaline, was a period of intense development of psychiatry and psychology. However, despite the rapid development of knowledge in the field of psychopathology or symptomatology, the scope of therapeutic effect was very limited. At first, the researchers tested mescaline on themselves to better understand the mechanisms of psychopathology and the direct experience of psychosis-like states. However, its usefulness in the treatment of mental disorders had not been considered, probably due to the dominance of psychoanalytic theories in the period described. It was only in the 1930s that Erich Guttman decided to investigate the therapeutic potential of mescaline, administering the substance to an unspecified group of subjects, both mentally ill and healthy. Guttman did not publish any objective results of his research, but he stated that the condition induced by mescaline could be useful in psychotherapy and could be the key to understanding the phenomenon of psychosis [9].

The 1950s should be considered as the beginning of the wave of intense interest in psychiatry with psychedelic substances. It was the time when the first psychotropic drugs were introduced in therapy and LSD was popularized among researchers who, under the trade name of Delysid, received it for free, encouraged to search for possible uses of this substance in medicine. After it had been proven that even high doses do not cause significant physiological side effects, LSD, psilocybin and mescaline started to be widely used for research in diverse populations of patients with mental disorders. Psychedelics were administered to subjects suffering, i.a., from personality, affective, anxiety, obsessive-compulsive disorders, post-traumatic stress disorder (PTSD), addiction to alcohol and other substances, and schizophrenia [8]. In addition, psychologists and psychiatrists considered them as a "tool to shorten psychotherapy" [10]. There was an increasingly common belief that these substances could be another major breakthrough in psychiatry. However, it was quickly observed that psychedelics not only

did not improve the condition of psychotic patients, but often taking them could lead to exacerbation of disease symptoms. Test results in groups of patients with anxiety and depressive symptoms were much more promising. A recent meta-analysis of 19 studies using psychedelics conducted between 1949 and 1973 showed that almost 80% of patients suffering from unipolar depression experienced clinical improvement [11]. In another meta-analysis, a potentially beneficial effect of using LSD in the treatment of alcohol addiction has been found [12].

Research from that period was characterized by a number of constraints or even methodological errors, which significantly affects the reliability of the obtained results and their usefulness for contemporary considerations. The most common issues were the following: inadequate or inconsistent selection of groups of respondents, inconsistent administration of treatment between groups, frequent lack of control groups and blanks, no validation of the results, documenting the results in an incomplete or inconsistent manner, frequent lack of information on the side effects, no statistical analysis of the obtained results [13]. Nonetheless, from the first wave of experiments using psychedelics in psychiatry, a picture emerges of substances with a safe pharmacological profile and therapeutic potential in treating depressive and anxiety disorders as well as addictions. Despite this, further research, necessary for the possible inclusion of psychedelic substances in psychiatric treatment, could not be continued and in the second half of the 1970s all significant work on this subject ceased. There were several factors which contributed to this situation.

Psychedelics not only aroused interest in the scientific world, but they also quickly gained on popularity in the wider society as recreational drugs, becoming an important part of the pop culture that existed at the period. LSD, having the reputation of a drug that "opens the mind," began to be associated with many subcultures, including the emerging hippie and psychedelic culture. These tendencies, along with the civil rights movement, sexual revolution or opposition to the Vietnam War, contributed to the phenomenon of counter-culture, the result of which were the rapid social changes shaking Western societies in the 1960s and 1970s. They also affected the countries on the other side of the Iron Curtain. These events aroused strong opposition of the conservative part of society, including many influential politicians, media decision-makers as well as medical authorities. The media began to print alarmist articles scaring public opinion with a new, deadly threat to the young generation. Often the real negative consequences of the abuse of psychedelic substances in susceptible individuals were exaggerated. The reported cases of persistent changes in perception in people who had been using LSD or psilocybin in the past were classified as the "Hallucinogen Persisting Perceptual Disorder."

Reports of cases of unethical medical experiments using psychedelics or CIA's efforts to use them as a "serum of truth" or biological weapon contributed to further stigmatization [14]. As a consequence, in 1967 psychedelic substances were entered in Schedule I of the UN's Single Convention on Narcotic Drugs, which resulted in a ban on their manufacture, possession and use.

The proverbial nail in the coffin of research using psychedelic substances was the tightening, as a result of the "Thalidomide tragedy," of regulations concerning the introduction of new drugs to the US market in 1962. [15]. This decision coincided with the loss by Sandoz of the Delysid patent, which combined with the growing controversy surrounding the topic, made further experiments with psychedelics less profitable in financial terms.

When in 1971 US President Richard Nixon announced the beginning of the "war on drugs," the fate of research into the use of psychedelics in medicine seemed sealed.

The second wave of research – current state of knowledge

The renaissance of scientific research on psychedelic substances took place in the 1990s along with a new generation of researchers and a gradual change in the socio-political attitudes towards drugs, which resulted in an increasingly clear questioning of the legitimacy of continuing the "war on drugs" [16]. As a result, 3 works emerged studying the effect of psychedelics on healthy volunteers: mescaline in Germany [17], dimethyltryptamine in the United States [18] and psilocybin in Switzerland [19]. In the following years, studies on the psychedelic state in volunteers unburdened with mental illnesses in terms of neuroimaging [20, 21], psychopharmacology [21, 22] and neuropsychology [23] were published.

For the needs of this study, a review of the literature available in the PubMed database was made. The materials used in the publication were obtained by searching the PubMed database for the following phrases: "psychedelics," "hallucinogens," "psilocybin," "LSD," "Lysergic acid diethylamide," "DMT," "ayahuasca," "N,N-dimethyltryptamine," and "mescaline." Materials published in the years 1936–2018 were analyzed. Peer-reviewed articles reporting only clinical trials were analyzed over the past 25 years. The participants of the study had to meet the diagnostic criteria from the group of anxiety, depressive, or addiction disorders according to the DSM-IV classification. All the studies described assumed the use of psychedelic substances exclusively under strictly controlled experimental conditions. The differences in the scope of symptom severity were each time measured using standardized diagnostic scales.

Obsessive-compulsive disorders (OCD)

In an open clinical trial in 2006, 9 patients diagnosed with OCD according to DSM-IV, with a history of at least one ineffective therapy using selective serotonin reuptake inhibitors (SSRIs), were orally administered up to 4 doses of psilocybin. All patients received a low dose (100 μg/kg) of the compound during the first session, during the subsequent ones the dose was to be increased to the average (200 μg/kg) and then high (300 μg/kg). However, starting from the second session, the patient could randomly receive either an increasing or very low dose (25 μg/kg). The sessions were separated from each other in time by at least a week. The worsening of OCD

symptoms was studied using the *Yale-Brown Obsessive-Compulsive Scale* (YBOCS) immediately after taking the substance and 4, 8 and 24 hours later, respectively. All subjects received low doses of the substance, seven very low and medium, and six – all of them. Reduction of symptoms' severity, according to the YBOCS by 23–100%, was observed during one or more sessions. 88.9% of subjects maintained an improvement of at least 25%, and 66.7% by at least 50% within 24 hours of receiving at least one dose of psilocybin. Two participants of the study declared symptomatic improvement one week after taking the last dose, one – after 6 months. However, there was no correlation between the clinical improvement scale and the adopted doses of psilocybin. No significant side effects were observed [24].

Anxiety and depressive disorders related to directly life-threatening diseases

In 2011, a randomized, double-blind clinical trial was performed on 12 people suffering from an advanced stage cancer and one of the following diagnoses under DSM-IV: acute stress response, generalized anxiety disorder, an anxiety disorder caused by cancer, and adaptive disorders with dominant anxiety. Each subject received 200 μg/kg bw of psilocybin or 250 mg of niacin during a single session. *Beck Depression Inventory* (BDI), *State-Trait Anxiety Inventory* (STAI), and *Profile of Mood States* (POMS) were used to measure the worsening of symptoms. The first measurements were made the day before, the day after and 2 weeks after the session. Next, the patients were examined every month during a six-months follow-up. All of the participants took part in the study for at least 3 months, eleven – for 4, and eight completed a full 6 months of observation. During the experiment, 2 subjects died from cancer, and the condition of the next 2 worsened so much that they were unable to continue the experiment. Significant improvement was observed according to STAI after 1 and 3 months and in BDI after 6 months from completion of the study. There were no changes in the POMS scale. Psilocybin was well tolerated by all participants in the experiment [25].

A similar study on a group of 12 patients using LSD was carried out in 2014. In addition to cancer, the subjects suffered from chronic inflammatory or motor system diseases. In addition, this group was diagnosed with a major depressive episode, reactive depression, dysthymia, post-traumatic stress disorder, panic disorder, or social phobia according to DSM-IV criteria. The experiment was composed of standard psychotherapeutic sessions and two LSD-assisted psychotherapy sessions. The subjects initially received 200 μg of LSD or active placebo – a type of placebo that causes perceived side effects the purpose of which is to convince the test subject that he or she receives the substance that is the subject of the experiment. In the described case it was a very low LSD dose – 20 μg. After 2–3 weeks, those patients who received the placebo were offered an experimental dose of LSD (200 μg). Elevation of anxiety symptoms was measured using the STAI questionnaire one week after the LSD session and after 2 and 12 months. After 2 months, a statistically significant decrease in the severity of state anxiety and a trend toward reducing the severity of trait anxiety was found. Lower

results in the STAI questionnaire as opposed to the initial state were still maintained 12 months after the LSD session. No serious side effects were reported [26].

Two further studies using psilocybin in a group of patients suffering from anxiety and depressive disorders associated with cancer were carried out in 2016. Both were in the form of a randomized crossover study. In the first one, carried out on a group of 51 subjects, the patients had two sessions with psilocybin, obtaining a high (22 mg/70 kg or 30 mg/70 kg) or low (1 mg/70 kg or 3 mg/70 kg) dose of a compound (an active placebo). Depending on the dose of psilocybin taken during a given session, the patients were either a treatment or a control group. After 6 months, 78% of subjects reported clinically significant reduction in symptoms, and 65% – remission of depressive symptoms measured by the *Hamilton Depression Rating Scale* (HAM-D). Measurements performed using the *Hamilton Anxiety Rating Scale* (HAM-A) showed a reduction in the symptoms in 82.5% of subjects and remission of symptoms in 56.5% of patients taking part in the experiment. The difference in the obtained results when using a low and high dose of psilocybin was statistically significant. There was also statistically significant improvement in areas such as general quality and meaning of life, the level of optimism or fear of death.

In the second study, 29 patients received a 0.3 mg/kg dose of psilocybin or 250 mg of niacin as an active placebo during 2 two-hour psychotherapeutic sessions. Within 4 months, before, between, and after receiving the substance, the patients also had 3 two-hour sessions of conventional psychotherapy (a total of 18 hours), followed by several sessions of supportive therapy during a 6 and a half months follow-up. Changes in symptom severity were assessed using the BDI, STAI and *Hospital Anxiety and Depression Scale* (HADS) scales 1 day before and after the first dose, 2 and 6 weeks after the first dose, 7 weeks after the first dose (= 1 day before the second dose) and 1 day, 6 and 26 weeks after the second dose. Seven weeks after the first dose of psilocybin, the results obtained in BDI decreased by at least a half in 83% of subjects, and the severity of anxiety symptoms measured by HADS was 58%. No improvement was reported after taking only niacin, before taking psilocybin during the next session. Overall, after six and a half months of the study, clinically relevant reductions in anxiety or depressive symptoms were observed in approximately 60–80% of patients.

In both these studies the occurrence of mystical experiences measured by the *Mystical Experience Questionnaire* (MEQ30) positively correlated with positive therapeutic effects. No significant adverse reactions were reported in the subjects [27, 28].

Addictions

In 2014, an open clinical trial was carried out using psilocybin on a group of 15 patients addicted to nicotine, who had not been suffering from any other accompanying mental disorders. The volunteers had been smoking 19 cigarettes a day for 31 years on average and had already made six attempts to stop smoking. Each of them participated

in a 15-week therapy for the treatment of tobacco addiction (in cognitive-behavioral therapy, CBT). The subjects received psilocybin in the 5th, 7th and 13th week of therapy. During the first session with psilocybin, each participant of the study was administered a moderate dose of the substance (20 mg/70 kg), during the next two sessions the subjects could choose whether to remain with the moderate dose or take a high dose of psilocybin (30 mg/70 kg). For 6 months after taking the psychedelic, both the patient's declarations and biological markers were evaluated weekly. At the end of the study, 80% of participants remained abstinent. In addition, a significantly reduced nicotine craving and temptation to return to the habit of smoking were observed throughout the duration of the measurements, and the participants' beliefs about abstinence continued to decline after reaching the peak one week after the first session with psilocybin. No significant side effects were observed [29].

In another open-label trial, a group of 10 patients with a history of an average of 15-year addiction to alcohol was subjected to standard Motivational Enhancement Therapy (MET) for a period of 12 weeks. In addition, each volunteer at an interval of 4 weeks underwent 2 sessions supported by psilocybin (0.3 mg/kg or 0.4 mg/kg). The patients' condition was assessed prior to the first therapeutic session and 36 weeks after the beginning of the study. A statistically significant reduction in the number of heavy drinking days (defined as daily consumption of 4 or more alcoholic drinks containing 14 g of ethanol) was demonstrated. There was a positive correlation between the scale of clinical improvement and the psychedelic potency during the session. Psilocybin was well tolerated by the subjects [30].

Depressive disorders

In recent years, an attempt has been made to use psychedelic substances in treating major depressive disorders. In the 2015 pilot study, a group of 6 subjects was administered 2.2 ml/kg of Ayahuasca containing 0.8 ml/kg of DMT and 0.21 ml/kg of harmaline (MAO inhibitor, which by preventing DMT metabolism in the periphery enables its penetration to the brain). All subjects suffered from recurrent depressive disorders and had never used Ayahuasca before. The severity of the depressive symptoms was assessed using the HAM-D and *Montgomery-Asberg Depression Rating Scale* (MADRAS) before administration of the substance and 1 day, 1, 2 and 3 weeks after taking the psychedelic drug. There was a statistically significant reduction in symptom severity in all measurements, except for a study which was carried out 2 weeks after the DMT session.

The experiment was carried out in an extended way a year later in the form of an open-label trial on a group of 17 volunteers with the same characteristics as before. The subjects received the same dose of ayahuasca, and the 3-week observation confirmed the results obtained previously – a statistically significant reduction in the severity of depressive symptoms assessed with the HAM-D and MADRAS scales. No serious side effects were observed at any stage of the study [31, 32].

Another open-label trial, carried out in 2016, tested the potential use of psilocybin in antidepressant therapy. The study group consisted of 20 volunteers diagnosed with drug-resistant depression, at the time of moderate to severe depression, without psychotic symptoms. Each one of them was given 2 doses of psilocybin (a "test dose" of 10 mg and a "therapeutic dose" of 25 mg), each time with psychological support before and after the experiment with psychedelics. The patients self-assessed the severity of depressive symptoms using the QIDS (*Quick Inventory of Depressive Symptomatology*) scale before taking the first dose of the substance and one week after the second session with psilocybin, and then for the next half a year. A significant reduction of the symptoms was observed after 1, 2, 3, and 5 weeks (maximum effect), as well as in measurements made after 3 and 6 months since the last session. Five patients received an additional dose of the psychedelic at their own request, which may affect the results obtained in the 3rd and 6th month of the study. No serious side effects were observed during the experiment [33, 34].

In 2018, a group of Brazilian researchers published the results of another study that evaluated the antidepressant properties of Ayahuasca. It was the first experiment with the use of a psychedelic to meet the criteria of a randomized double-blinded clinical trial. The inclusion criteria included the diagnosis of a major depressive disorder according to DSM-IV (mean duration of the disease – 11 years), confirmed drug resistance (4 ineffective drug therapies on average), severity of the current episode from moderate to severe, absence of psychotic symptoms, no history on ayahuasca use in the past. Finally, 29 people were qualified and divided into a study group (n = 14) and a control group (n = 15). A solution of water, yeast, citric acid, zinc sulfate, and caramel dye was used as a placebo, which imitated the color and taste of Ayahuasca and caused gastrointestinal complaints characteristic of the oral use of this psychedelic drug. Two weeks before the administration of the substance to all experiment participants, the antidepressants taken so far were discontinued. The patients in the study group received Ayahuasca containing an average of 0.36 mg/ml of DMT and MAO inhibitors: 0.11 mg/ml of harmine, 0.24 mg/ml of harmaline and 1.20 mg/ml of tetrahydroharmine. The volume of the solution was adjusted so that every volunteer in this group received 0.36 mg/kg of DMT. In the control group, each patient received 1 ml/kg of the placebo. The severity of depressive symptoms was measured using the MADRAS scale before, 1, 2, and 7 days after the session with Ayahuasca and HAM-D before and 7 days after taking the psychedelic. In both of these scales a statistically significant reduction in the severity of the disease symptoms was found. The difference between the improvement range between the treatment and control group was also statistically significant and increased over time. Ayahuasca was well tolerated by the volunteers [35].

Limitations and problems to be solved

Despite the promising results of experimental clinical trials, the prospect of using psychedelics as drugs for psychiatric treatment remains remote. Apart from the limitations typical of most substances at an early stage of testing (including small, not very demographically different groups of subjects, risk of too optimistic interpretation of results), a number of problems specific to this group of substances exists. The most important of them include:

- diversified and not entirely explained molecular mechanism of action – all "classic" psychedelics are 5-HT2A serotonin receptor antagonists; however, they differ significantly in the range of their impact on other systems of neurotransmitters. On top of that, there is a high variability in the strength and duration of action of identical doses of individual substances in different users;
- the specificity and subjectivity of experiences – the intensity and uniqueness of the psychedelic experience definitely constraints the possibility of creating some reliable measurement criteria. Previous attempts to determine the relationship between the strength of "mystical experiences" and the therapeutic effect gave ambiguous or contradictory results. Moreover, this experience may be too overwhelming for some users (the so-called "bad trip"), so it seems reasonable that each psychedelic session should be accompanied by a trained assistant/carer providing patients with the necessary (psychological) support;
- difficulty in obtaining a blinded experiment – the way psychedelics work and the universality of ideas about their effect in pop culture significantly hinder the selection of a reliable placebo. A partial solution may be to use very small doses of the substance under study in this role;
- the risk of triggering or exacerbating psychotic disorders – pre-Prohibition studies have shown that psychedelic substances can exacerbate symptoms in patients suffering from psychotic disorders. Although in the course of modern tests, there were no reported cases of prolonged psychotic states or disturbances of perception caused by hallucinogens, but patients with psychotic history (personal or family) were excluded from them. Negative selection of volunteers with an increased risk of psychosis seems to be the necessary limitation of any further clinical trials;
- safety – no serious side effects had been observed in the course of previous studies after taking psychedelic substances. However, relatively common side effects include: blood pressure increase, tachycardia, arrhythmias, increased body temperature, headaches, and nausea. This may limit the potential group of psychedelic therapy beneficiaries;
- the influence of psychotherapy – in part of the studies from the second wave, sessions with psychedelic substances were accompanied by some form of psychotherapy. The issue to be resolved is to what extent psychotherapeu-

tic interactions are responsible for the positive clinical effects of psychedelics and whether these substances can be used as an independent form of therapy;

– legal restrictions and commercial potential – psychedelic substances are still included in Schedule I of the UN's Single Convention on Narcotic Drugs, which in most countries results in a ban on their manufacture, possession and use. This fact obviously constraints the possibilities of conducting large-scale clinical trials and the possible use of psychedelics in pharmacotherapy. The difficulties described above may negatively affect the interest of pharmaceutical companies in investing in further research – after the expiry of patents on LSD and psilocybin, the costs of obtaining their re-registration may outweigh the potential benefits. However, the already noticeable changes in the attitude of public opinion and the scientific and medical community towards psychoactive substances give hope for changing these unfavorable circumstances in the future [36].

Conclusions

The health, social and economic consequences of diseases and mental disorders are becoming an increasing burden for contemporary societies. The scale and intensity of this problem, without a hint of exaggeration, allow us to talk about a crisis that is likely to continue growing in the future. Available therapeutic strategies seem to be insufficient, and the development of new drugs in psychiatry has slowed down for some time [37]. The search for alternative approaches and solutions is becoming a must.

Studies carried out so far indicate that psychedelic substances may be used in the treatment of depressive disorders, anxiety disorders, addictions, or psychological difficulties in the face of dying and death. Moreover, there are reports suggesting the possibility of using psychedelics to facilitate the psychotherapeutic process [38] or their beneficial influence on reducing the risk of suicidal and criminal behavior [39, 40].

Obviously, at this moment we have only preliminary results at our disposal. Without reliable, large-scale tests, it is impossible to verify the real potential of using psychedelic substances in psychiatry. In addition, the amount and complexity of problems to be solved may raise reasonable doubts as to the profitability of conducting further research in this direction. Nonetheless, in the face of the global crisis of mental health, the costs of hasty rejecting this perspective may turn out to be incomparably higher.

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