Chapter 82

Psilocybin as an Inducer of Ego Death and Similar Experiences of Religious Provenance

Katarzyna Stebelska[1], **Krzysztof Łabuz**[2]

[1]Department of Analytical and Ecological Chemistry, Faculty of Chemistry, Opole University, Opole, Poland; [2]Unit for Treatment of Addiction, Sahlgrenska University Hospital, Gothenburg, Sweden

Abbreviations

5-HT 5-Hydroxytryptamine
5-HT$_{1A}$, 5-HT$_{2A}$ 5-Hydroxytryptamine receptors, types 1A and 2A
ACTH Adrenocorticotropic hormone
APZ "Abnorme Psychische Zustände," translated as "Altered State of Consciousness Scale"
DMN Default-mode network
DP1 Prostaglandin D2 receptor
fMRI Functional magnetic resonance imaging
GPR109A G-protein-coupled receptor 109A, niacin receptor 1
NMDA-R *N*-Methyl-D-aspartate receptor
NO Nitric oxide
PET Positron emission tomography
PGD2 Prostaglandin D2
PLA2 Phospholipase A2
PRL Prolactin
TAAR1 Trace amine-associated receptor 1
TSH Thyroid-stimulating hormone

INTRODUCTION

The altered states of consciousness reached after ingestion of psychoactive herbs or by the use of other techniques served in shamanistic cultures to contact divine beings and in initiative rituals, which allowed an adolescent to join the adults of a tribal society. The rituals were usually difficult to survive and served to maintain the closed nature of the tribal community and to force obedience or subordination to the group; thus, the group conserved and reproduced its culture in all aspects, making social and technological development more difficult. More modern religious systems still contain some elements of initiative rituals. Fixation around death in the present-day systems of beliefs, particularly in Christianity, mirrors near-death experiences of primal rites of passage. Similarly the Eucharist ceremony symbolically represents the practices of sacramental ingestion of psychoactive herbs very common to shamanistic cultures. Therefore old shamanistic practices of intoxication with herbal neurotoxins (stimulants, hallucinogens, dissociatives, or deliriants) easily spread over new syncretic cults containing elements of Christianity and also beyond the religious movements as a part of prison subcultures and a custom of recreational use of drugs (Halpern & Sewell, 2005). Several examples of inebriants used for religious purposes are presented in Table 1. The inebriants traditionally used within tribal societies have become interesting to a developing Western science and have been applied for the purposes of an economy based on agriculture.

One of the best known entheogens is psilocybin—a hallucinogenic indolealkylamine naturally occurring in fungi of the *Psilocybe* genus. This substance was studied as an inducer of mystical-type experiences in religiously inclined individuals (Doblin, 1991; Griffiths et al., 2011; Griffiths, Richards, Johnson, McCann, & Jesse, 2008; Griffiths, Richards, McCann, & Jesse, 2006; MacLean, Johnson, & Griffiths, 2011). In the United States the hallucinogen, thought to be safe, nontoxic, and nonaddictive, is being considered to be used in psychotherapy. It should be mentioned here that hallucinogens have already been applied in so-called psycholytic therapy derived from psychoanalysis mainly to improve access to the unconscious content of memory and primitive emotions of a patient (Leuner & Holfeld, 1962). Such treatment is not necessarily associated with the patient's good frame of mind during the drug session because spontaneous or drug-facilitated recollection of memories usually involves posttraumatic experiences. Additionally psilocybin transiently impairs cognitive functions, exposing a patient to excessive domination or even abuse from a therapist. Today attention is being paid to transient and potentially persistent mood improvement resulting from psilocybin experience. Psilocybin has been shown to improve the recollection of personal memories in a functional magnetic resonance imaging study (the participants were asked to recollect only positively experienced memories) (Carhart-Harris, Leech, et al., 2012). Psilocybin was also shown to reveal some, probably paradoxical, potentially mood-improving effects resulting from emotional bias in healthy subjects (Kometer et al., 2012; Schmidt, Kometer, Bachmann, Seifritz, & Vollenweider, 2013) and in terminal-stage cancer

TABLE 1 Herbs Containing Psychoactive Compounds Used in Religious Practices

Natural Source of Psychoactive Compound	Psychoactive Compound	Religious System, Culture
Cannabis	Tetrahydrocannabinol	Hinduism, Buddhism, Judaism and Christianity (mentioned in the Bible texts), Islam, more contemporary syncretic cults with elements of Christianity, animism, and Hinduism such as the Rastafari movement, prison subcultures
Jimsonweed (*Datura stramonium*) and other members of the genus *Datura*, henbane (*Hyoscyamus niger*), belladonna (*Atropa belladonna*), mandrake (*Mandragora officinarum*)	Hyoscine and hyoscyamine	Hinduism, Buddhism, pre-Columbian Aztecs, initiative rituals of North American Indians
Psilocybe mushrooms (*Psilocybe mexicana*, *Psilocybe caerulescens*)	Psilocybin, psilocin	Pre-Columbian Aztecs and Mayan people, at present certain Mexican tribes (in the Mazatecs the rituals of the mushroom's ingestion are typical shamanistic practices strongly influenced by Christianity)
Ska Pastora (*Salvia divinorum*)	Salvinorin A	The Mazatecs (shamanistic training and ceremonies)
Morning glories (*Rivea corymbosa*, *Ipomoea violacea*)	Ergine	Pre-Columbian Nahuas and Aztecs, Mexican tribes: the Chinantecs, the Mazatecs, the Mixtecos, and Zapotec people
Peyote buttons (dried crowns of *Lophophora williamsii*)	Mescaline	Pre-Columbian Mexican Indians (the Toltecs, the Chichimecs, the Aztecs) and their descendants, North American Indians (peyotism, syncretic religion containing elements of Christianity, has become the most popular religion among North American Indians)
Ayahuasca, a brew containing leaves of a forest vine *Banisteropsis caapi* with certain herbal additives, such as leaves of *Psychotria viridis* or *Psychotria carthaginensis*, bark of *Virola* trees, beans of *Anadenanthera peregrina*, leaves of *Banisteropsis rusbyana*, *Justicia pectorialis*	*N*,*N*-dimethyltryptamine, bufotenin, 5-methoxy-*N*,*N*-dimethyltryptamine, harmine, harmaline, tetrahydroharmine	South American shamanism, syncretic cults influenced by Christianity developing in South America, such as Santo Daime, União do Vegetal, and Barquinha
Tobacco (*Nicotiana rustica*, *Nicotiana tabacum*)	Nicotine, β-carbolines	South American shamanism, Nahuas, prison subcultures
Fly agaric (*Amanita muscaria*)	Ibotenic acid, muscimol	Syberian shamanism (Koryak people, Chukchi people, Yukaghir people, Selkup people, Nenets people, Nganasan people, Khanty people, Mansi people, the Kamchadals, the Kets), North American Indians Fly agaric, which is not a deadly poisonous mushroom like some other members of the *Amanita* genus, was probably an object of primitive phallic cults because of the phalloid shape of the fruit bodies at the early stage of development. It is possible to evoke hallucinations after drinking urine from an intoxicated subject. The practice of urine drinking to become intoxicated, observed in half-wild reindeers and used to handle the animals, could then become a kind of unity ritual in Syberian shamanism. Fly agaric is linked also to Hinduism and possibly to early Christianity.
Iboga shrub (*Tabernanthe iboga*)	Ibogaine	Initiative rituals in Bwiti religious movement The origin of the Bwiti movement is uncertain; since it incorporates African animism, elements of Christianity, and a cult of white ancestors, it was possibly inspired by colonial authorities. At present Bwiti is worshipped by the Babongo and the Mitsogo peoples of Gabon and by the Fang people of Gabon and Cameroon.

Examples of herbal psychoactive substances utilized for religious purposes (initiative rituals, shamanistic ceremonies and training, to induce hallucinations or emotional phenomena) are presented.

patients (Grob et al., 2011). However, the same substance was proven to induce a psychotic state very similar to schizophrenic psychosis, mimicking also some cognitive deficits observed in schizophrenia (Carter et al., 2005; Gouzoulis-Mayfrank, Schreckenberger, et al., 1999; Gouzoulis-Mayfrank, Thelen, et al., 1999; Gouzoulis-Mayfrank et al., 2002; Spitzer et al., 1996; Umbricht et al., 2003; Vollenweider, 2001; Vollenweider, Csomor, Knappe, Geyer, & Quednow, 2007; Vollenweider et al., 1997; Vollenweider, Vollenweider-Scherpenhuyzen, Bäbler, Vogel, & Hell, 1998; Vollenweider, Vontobel, Hell, & Leenders, 1999). Thus, this now very well described compound links schizophrenia-like psychosis and religion.

THE CONNECTION BETWEEN SCHIZOPHRENIA-LIKE PSYCHOSIS AND RELIGIOUS EXPERIENCES

Psychosis has already been compared to mystical experiences, starting from Freud's conceptualization of religious inclination as a form of neurosis (Cariola, 2012). More modern psychoanalysis very quickly adapted new discovered hallucinogenic drugs and implemented them in therapeutic practice for diagnostic purposes despite their psychedelic activity (Leuner & Holfeld, 1962; Naranjo, 1969).

The concept of drug-induced model psychosis is not new and it used to be regarded as an adequate tool for modeling of acute psychosis and schizophrenic psychosis (Gouzoulis-Mayfrank, Hermle, Thelen, & Sass, 1998; Vollenweider, 2001). Acute psychosis induced by drugs and schizophrenic psychosis may share similar neurochemical backgrounds and biologically conditioned individual susceptibility—an example could be dopamine β-hydroxylase gene polymorphisms implicated in the development of both methamphetamine-induced psychosis and schizophrenia (Chen et al., 2005; Okahisa et al., 2014). Examples of drugs able to produce psychosis comparable to schizophrenic psychosis are presented in Table 2.

Schizophrenia belongs to the endogenic psychoses, although many drugs are known to worsen preexisting schizophrenia (e.g. phencyclidine, ketamine, stimulants improving dopamine release or levodopa). Schizophrenia develops within years, most often

TABLE 2 Psychoactive Drugs Able to Induce Schizophrenia-Like Psychosis

Compound	Class of Psychoactive Substance	Symptoms of Psychosis	References
Mescaline	Hallucinogen, agonist at 5-HT_{2A}, probably able to activate adrenergic receptors	Intense visual and auditory hallucinations usually connected to past mental experience, increased emotionality and suggestibility, dysphoria, sleep deprivation, cognitive deficits	Stockings (1940)
Lysergic acid diethylamide (LSD)	Hallucinogen, agonist at 5-HT_{2A}	Hallucinations, delusions, mood swings, panic attacks, long-lasting changes in central nervous system leading to appearance of so-called "flashbacks" (hallucinogen persisting perception disorder)	Halpern and Pope (2003)
Bufotenin, dimethyltryptamine	Hallucinogens, agonists at 5-HT_{2A} (hallucinogenic action) and 5-HT_{1A} (possibly anxiolytic action), ligands of trace amine receptors	Visual and auditory hallucinations, synesthesias, mood swings, helplessness, working memory impairments Endogenously produced substituted tryptamines were proposed to be involved in the development of psychosis in schizophrenia.	Ciprian-Ollivier and Cetkovich-Bakmas (1997)
Phencyclidine, ketamine	Dissociatives, antagonists at NMDA-R	Anxiety, symptoms of ego dissolution such as depersonalization and derealization, hallucinations and delusions, dissociative states, grandiosity, hostility, blunted affect, emotional withdrawal, thought disorder, and cognitive deficits dependent on frontal cortical dysfunctions and affecting complex intellectual functioning such as planning and decision-making	Javitt (2007), Krystal et al. (1994), and Vollenweider (2001)
Amphetamine, methamphetamine	Stimulants, agonists at TAAR1; activation of this receptor inhibits or reverses transporters of dopamine, norepinephrine, and serotonin. Methamphetamine is an agonist of adrenergic receptor 2 and a MAO inhibitor.	Euphoria, paranoia, delusions of persecution or grandiosity, auditory hallucinations of content supporting persecutory delusions, anxiety, agitation, aggression, compulsive behaviors	Ciccarone (2011)

Continued

TABLE 2 Psychoactive Drugs Able to Induce Schizophrenia-Like Psychosis—cont'd

Compound	Class of Psychoactive Substance	Symptoms of Psychosis	References
Tetrahydrocannabinol	Cannabinoid, activates inhibitory cannabinoid receptor 1, by induction of proinflammatory pathway may increase brain level of kynurenic acid, which is an antagonist of the NMDA-R	Mild euphoric and stimulant effects (improved mood, sociability, relaxation, and decreased anxiety, alertness, and tension), alternations of spatial and temporal perception, intensification of sensual experiences, hallucinations (rarely at high doses), impairment of short-term memory, increase of reaction time, anxiety, depression, low motivation, delusions, derealization, dysphoria, paranoia, panic attacks Cannabis-induced psychosis increases risk of schizophrenia development.	Johns (2001)

The typical drugs that are known to produce psychosis, acute symptoms of intoxication, and long-lasting effects of repeated intake or abuse (including increased risk of schizophrenia development) are presented. NMDA-R, *N*-methyl-D-aspartate receptor; TAAR1, trace amine-associated receptor 1; MAO, monoamine oxidase.

during adolescence, because of prolonged improper functioning of the brain neurological system exposed to destructive agents of a psychological nature. Interestingly, schizophrenia came to be diagnosed as a distinct disease (although numerous phenotypic variants of the disease exist) at the end of the nineteenth century—the disease, named at that time "dementia praecox," typically affected young men (Jablensky, 2010). The first symptoms of the disease, namely anxiety and depression, are nonspecific. The prodromal phase is dominated by negative symptoms and cognitive deficits (Table 3). The acute psychosis stage is additionally manifested by positive symptoms (Table 3).

All negative symptoms of schizophrenia are somehow tightly connected to poor-quality social relations. The positive symptoms also mirror difficulties in social adaptation. Delusions of persecution and thought control are often present in schizophrenia. The delusions, if religious in essence, may concern being sinful and guilty, and together with auditory hallucinations ("hearing voices"), very common in schizophrenia, they reflect the oppressive character of the community to which the schizophrenia-suffering individual belongs. Psychotic symptoms of incomplete ego boundary formation or ego disintegration, common to schizophrenics (Lerner, Sugarman, & Barbour, 1985), partly result from the intrusive character of the surrounding social environment. Thus, the etiology of schizophrenia is complex, including genetic, environmental, and perinatal factors; neurodevelopmental disturbances; and psychosocial prerequisites.

Communities conglomerated around any religious cult may be particularly dangerous for the mental health and proper development of personality in adolescent individuals (Barabasz, Hyrnik, Janas-Kozik, & Jelonek, 2012; Dein & Littlewood, 2011). Participation in religious rituals, particularly if collective, may become dominated with negative emotions, such as terror, shame, and sense of guilt. Simultaneously religious cults, particularly if containing elements of Christianity, offer a kind of symbolic emotional compensation: absolution, salvation, sacramental "rewards" expressed in a gesture of feeding. Therefore participation in religious ceremonies may evoke a kind of psychological regression and induce brain mechanisms of the reward system involving dopamine release within the mesolimbic and mesocortical dopamine pathways. Schizophrenic psychosis never develops before puberty and it seems like hidden pornographic motifs contained in religious beliefs may increase a risk of the disease, because the reward system is also involved in sexual emotionality. Monumental architecture and ornamentation of temples as well as religious scriptures surrounding worship mythically form together a kind of semantic network enabling the spread of associations in previously designed directions. According to some authors schizophrenia should be considered an aberrant salience disorder (Kapur, 2003; Van Os, 2009). The problem consists in excessive attribution of salience to neutral stimuli and possibly results from associative learning. The regimen of regular participation in religious ceremonies increases the probability of a similar phenomenon. Combining religious settings and intoxication with psychoactive substances may be extremely dangerous because psychosis-like states evoked to trigger mystical feelings, especially if associated with hallucinations, induce psychological regression comparable to dissociative phenomena along with abnormalities of cognitive functions, which further increase susceptibility to suggested messages.

TABLE 3 Typical Symptoms of Schizophrenia (Jablensky, 2010; Trémeau, 2006)

Negative symptoms	Avolition, isolation, social withdrawal, emotional blunting, anhedonia, restricted affect, decreased expression of emotions, lack of spontaneity, inability to keep visual contact, reduced mimicry and modulation of voice, difficulty to recognize emotions based on vocal modulation and facial expression
Cognitive deficits	Deficits in attention, confusion, poor speech and disorganized track of thoughts, both characterized with loosening of semantic associations
Positive symptoms	Disorders of perception and mood, alternations of motor activity, delusions, symptoms of ego disintegration, depersonalization and dissociative phenomena, auditory and visual hallucinations

The negative and the positive symptoms of schizophrenia along with cognitive impairments known to be associated with the disease are briefly summarized.

THE PHENOMENON OF EGO DEATH

Religious-type emotionality refers to a range of emotions developed and trained mainly in contact with the mythological content of the belief. The content is usually very rich and may be enjoyable but also disturbing, terrifying, and aversive. It may contain references to typically human aspects of life, as in Christianity; therefore even a child may find these fiction stories close to reality and try to identify with them. In Christianity the members of the cult are even encouraged to identify with the character of Jesus Christ and to think about themselves as God's children—this suggestion is easy to implement in children because of incomplete individuation and developing self-identity. References to childhood, and also to animals, since associative learning is a term close to Pavlovian conditioning originally described in an animal model, are surprisingly often in the Christian rhetoric. This may be not well tolerated in adults; however, it is practiced for some reasons. Children, owing to their vulnerability to infections and ongoing developmental processes, experience hallucinations, paresthesias, synesthesias, and alternations of body self-image more easily than adults and are more susceptible to suggestion owing to their insufficient immature intellectual functioning and ongoing formation of ego boundaries (Wigman et al., 2011). The conceptualization of Jesus Christ as God's child is in accordance with the already historical, early psychoanalytic concept of the id—the unconscious part of personality containing instinctual drives. References to morality and perfection identified with the divine being correspond to the concept of the superego—the structural part of personality containing a narcissistic idealization of the self. The combination of the two shapes the exact conscious part of personality able or unable to act efficiently in reality (if harm avoidance has developed as the main feature of the resultant personality pattern). The process of ego boundaries formation may never end successfully (that is why childhood is permanently mentioned in religious speeches). Religious ceremonies are usually collective and are directed by an authoritative leader. This is an additional reason for stress and frustration, particularly in male participants. The main purpose of these practices is to evoke emotional sensations, such as grandiosity, euphoria, depersonalization, and derealization. They all contribute to the phenomenon of ego death.

The emotional phenomenon of ego death usually follows transient euphoric states associated with delusions of grandiosity and symptoms of ego dissolution interpreted as a sensation of unity with others or with the Universe (God, Absolute) and consists in loss of these illusionary sensations. This experience is emotionally quite unpleasant and may have serious consequences in the future, including suicide ideations and suicidal attempts. It should be emphasized that the phenomenon of ego death is somehow similar to a transition from mania to depression in bipolar disorder, a psychiatric disease often affecting adolescents and associated with a high incidence of suicidal attempts. The excessive emotional training during religious indoctrination consisting in recollection of negative emotions, such as anxiety, fear, shame, and sense of guilt, serves mainly to develop the ability to experience ego death, although ego death is not fully analogous to any of the mentioned emotional sensations and is usually more unconscious, more sensual, and more irrational, perhaps comparable to a hysterical helplessness, disappointment, and frustration of a small child. A single ego death experience is usually considered unpleasant, but if repeated several times or emotionally "learned" it may be a source of specific satisfaction or astonishment, called "enlightenment," "illumination," or "revelation."

POSSIBLE CONSEQUENCES OF EGO DEATH PRACTICING FOR SOCIAL LIFE

Ego death is practiced in Hinduism and Buddhism—the society within the systems developed is characterized by traditional social stratification and low social position of women. The concept of ego death is also mirrored in the myth of Icarus (adapted in psychoanalysis to identify primary process thinking) and in Christian mythology, in a central event of this cult, the death of Jesus Christ. The reception of such phenomena like ego death in culture, providing also some "rationalizing" literary descriptions and reasoning, is usually positive. That is why criticism of the practices is not often. Such experiences are believed to teach how to distinguish between good and evil or to get rid of disadvantages of characters like egocentrism. However, the benefits from this heavy and often humiliating emotional training are doubtful. An individual pressed with such stressors has only limited possibilities to defend against disagreeable content. One possibility is to operate with a cultural symbolic apparatus, although cryptic references contained in the system of texts and abstract ideas may still be sufficiently intrusive to induce regression to schizoid stereotyped thinking even in well-educated subjects. Impairment of cognitive functions in the course of intoxication with hallucinogens makes this regression more probable. An individual may also develop different coping strategies (including rituals, obsessive and compulsive behaviors) and defensive mechanisms. The psychological defense (consisting in projection, rationalization, or even dehumanization mechanisms), even if successful, may form attitudes directed against others; abnormalities of sexuality, misogyny, misanthropy; passive or aggressive antisocial behaviors, including terrorism; adaptive conformism; or even dissociation of personality to the extreme. Such circumstances make mind control possible but are not favorable for exploiting one's full potential. In such a culture, to transform an adolescent into an adult means to crush everything considered an illusion (thus prosperity, safety and well-being of others, and reality are regarded as less precious than transcendence). This transformation and the urgency to reproduce it in others may become a sadistic pleasure to those who are influenced by religious concepts, including ego death; who give up personal intellectual aspirations and are directed by resentments or other irrational motives (specifically understood justice, educational mission, and achievement of strategic objectives subordinated to the corporative group interests).

Well-educated members of modern Western societies may misunderstand the real nature of the ego death experience as well as the link between abuse of psychoactive substances and mental diseases or dysfunctions. It is worth mentioning here that hallucinogens, including psilocybin, have already been used as incapacitating agents. Hallucinogens are also not very popular in prison subcultures because, despite the fact that they enhance the imposition of prison behavioral and "moral" standards as a result of ego blurring, they simultaneously expose one to aggression. Within Western societies not only such serious chronic diseases as schizophrenia, but also any small impairment of cognitive functions or even transient physical weakness is often unacceptable. Therefore it is simply cruel to expose anyone's mental health to the risk of even transient impairment of cognition and intellectual functioning, because difficulties in interpersonal contact and disconnection of social relations may arise, affecting quality of life, preventing self-actualization, and increasing the probability of development of schizophrenia.

PSILOCYBIN-INDUCED PSYCHOSIS AND EGO DEATH

Cases of mystical-type phenomena, including ego death, that are spontaneous or induced by factors other than psychoactive substances are rare, and the possibility of facilitating their production with chemical compounds is very attractive. The extended research on historical texts and anthropological or ethnological studies concerning shamanistic cultures resulted in the rediscovery of many herbal inebriants used in a religious or cultural context. Ritual consumption of toxic plants or fungi, in which the American continents are very rich, for medicinal purposes or in religious practices, often regarded as spiritual healing, was common to pre-Columbian cultures (see Table 1). One such example is psilocybin mushrooms. According to the reports of Catholic missionaries the mushrooms were known to the Mayan people (under the name "xibalbaj okox," or "infernal mushrooms") and to the Aztecs (they called the fungi "Teonanácatl," or "flesh of God," and ingested them during religious rituals resembling the Eucharist in Christianity). This early terminology, probably influenced by Christianity, reflects the potential of psilocybin mushrooms to induce unpleasant experiences and insanity. From twentieth-century ethnographic studies it is known that the Mazatec Indians from Oaxaca, Mexico, collected fruit bodies of *Psilocybe caerulescens* for usage in partly medicinal, partly magical rituals called "vanadas." Such ritual was introduced to the American audience in *Life* magazine, in 1957 (Wasson, 1957). The first ever scientific experiment carried out to investigate the usefulness of psilocybin in religious practices took place very soon after that, in Boston, on Good Friday, 1962 (Doblin, 1991). Curiously enough, the experiment was designed in such a way that the substance used as an active placebo was niacin. Skin response to orally applied niacin is rapid and visible because it causes vasodilatation of superficial skin microvessels. Apart from the known fact that psilocin produces skin flushing and is an agonist of serotonin, normally a compound inducing both vasodilatation and vasoconstriction (psilocybin/psilocin vasoactivity is not expressed exclusively within the skin and may be important also for heart work and brain vasculature), the explanation of such a choice is not clear—according to the author it was done "to potentiate suggestion in the control subjects" (Doblin, 1991). Niacin skin reactivity depends mainly on phospholipase A2 and prostaglandin D2 activity and partly on serotonin release from platelets (Figure 1). An interesting detail may be that schizophrenic patients, particularly in the prodromal phase of the disease, are less sensitive to the niacin skin irritation test. The usage of niacin would be an easy method to eliminate schizophrenics from the control group and it seems like the authors of the Good Friday experiment could have been aware of the connection between religious emotionality and schizophrenia. Eventually they succeeded in proving the usefulness of psilocybin as an inducer of mystical type experiences (Doblin, 1991). Although the participants were administered a very high dose of psilocybin, namely 30 mg, all the physical side effects and negative emotions they experienced (fear of dying, fear of going crazy, 1 of 10 participants from the psilocybin group needed medicinal intervention with a tranquilizer during the experiment) could be attributed to the nature of mysticism or religious-type exaltation (Doblin, 1991). The data collected to form

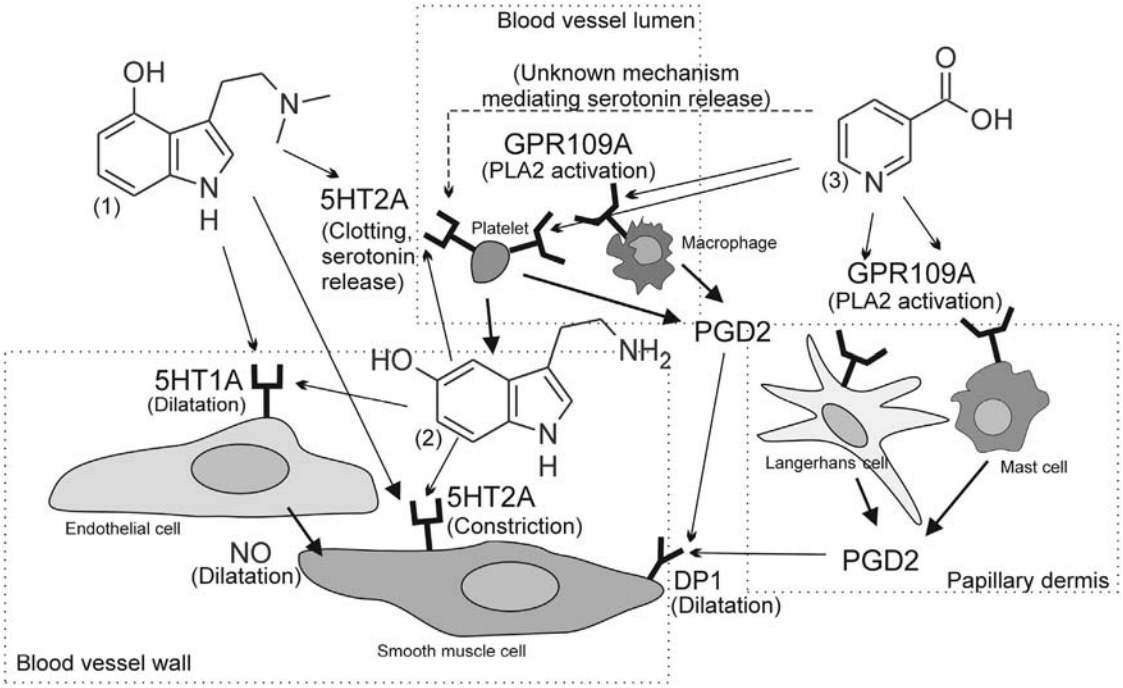

FIGURE 1 The mechanisms of (1) psilocin and (2) serotonin vasoactivity and (3) niacin-induced skin flushing. Psilocin and serotonin activate 5-HT_{1A} receptors located on endothelial cells. The ligation triggers production of nitric oxide, a potent vasodilator. Activation of 5-HT_{2A} receptors located on smooth muscle cells causes vasoconstriction. Niacin causes vasodilatation of dermal capillaries through activation of G-protein-coupled receptor 109A (GPR109A) located on the surface of dermal Langerhans cells, mast cells, macrophages, and platelets. Ligation of this receptor activates phospholipase A2 (PLA2) and leads to the synthesis of prostaglandins. Released prostaglandin D2 (PGD2) activates its receptor (DP1) on the surface of smooth muscle cells, leading to relaxation.

final conclusions about the results of the experiment were based on a 147-item questionnaire filled out 1 or 2 days later, long after all negative symptoms of intoxication subsided. Therefore the participants, who were religiously inclined theology students (probably with some anthropological knowledge), could "rationalize" their emotional experiences. This could be concluded also from their own descriptions of the psilocybin experience: after all they had survived, nothing wrong had happened, there was nothing to be afraid of, and the whole episode could be considered as something positive and inspiring, including having a positive impact on attitudes and social behavior (some of them would even recommend the use of psilocybin to their own children) (Doblin, 1991). However, in reality, drug-induced bad experiences, like other traumas, commonly evoke resentment, hostility, and antisocial attitudes often directed against new/younger/weaker members of the same group—this is a typical behavioral pattern among drug and alcohol abusers who try to propagate recreational usage of inebriants among adolescents because it is potentially harmful.

So-called "bad trips" happen usually after ingestion of high doses—above 15 mg. Oral administration of psilocybin at a dose equal to 0.224 mg/kg results in a peak plasma level of psilocin (8.2 ng/ml) after 105 min, coincident with the most intensified psychedelic effects (Hasler, Bourquin, Brenneisen, Bär, & Vollenweider, 1997). Usually doses between 10 and 15 mg and sensory deprivation (closed eyes, darkness) are enough to develop alternations of visual perception and pseudo-hallucinations in 1–1.5 h. Hallucinogenic activity occurs via activation of 5-HT_{2A} receptors without involvement of dopaminergic transmission (Vollenweider et al., 1998). Positively experienced depersonalization and emotional excitation are psychological effects after ingestion of doses around 15–20 mg (Hasler, Grimberg, Benz, Huber, & Vollenweider, 2004). Euphoric effects result from psilocybin-induced dopamine release in the striatum (measured with decreased binding of [^{11}C]raclopride) (Vollenweider et al.,1999). Higher doses intensify psychedelic effects, including unpleasant experiences (Hasler et al., 2004). The psychedelic effects of psilocybin intoxication are briefly summarized in Table 4. Participants in preliminary studies conducted in the early 1960s (Leary, Litwin, & Metzner, 1963) usually ranked psilocybin experiences as positive and pleasant (although very high doses were tested, up to 100 mg), but it was partly an effect of popularization of hallucinogens by members of the countercultural movement at that time. In addition, the drug dose is not the only predictor of the quality of experience—other factors, mainly psychological, are also involved. In their study Metzner, Litwin, and Weil (1965) found that dysphoric reactions to psilocybin appear in subjects who experienced negative mood and were preoccupied with personal problems before the drug intake. Pleasant experiences and visual effects were also less intensive in young persons and in subjects who declared having psychological problems prior to the drug session (Studerus, Gamma, Kometer, & Vollenweider, 2012). Neurotic patients (suffering from phobias or obsessions), whose reaction to psilocybin was dominated by anxiety, depersonalization, and aggression, often denied hallucinogenic effects (Delay, Pichot, & Lemperierie, 1963).

TABLE 4 Psychological Schizophrenia-Like Effects of Psilocybin

Category of Symptoms	Symptoms	References
Alternations of perception	Alternations of visual perception are the most pronounced effects. These are shape alternations, illusions of motion of stationary objects, body image distortions, elementary and complex hallucinations (usually pseudo-hallucinations), typically composed of kaleidoscopic patterns characterized with bright colors; images of human faces and characters, sometimes distorted, were also reported.	Malitz, Esecover, Wilkens, and Hoch (1960), Penden et al. (1981), and Vollenweider et al. (2007, 1997, 1998, 1999)
	Auditory effects in psilocybin-induced psychosis are not intense.	Halser et al. (2004)
	Synesthesias and paresthesias were reported.	Gouzoulis-Mayfrank, Thelen, et al. (1999), Griffiths et al. (2011), Hasler et al. (2004), Hollister (1961), and Malitz et al. (1960)
	Time perception is affected after psilocybin ingestion.	Hasler et al. (2004), Malitz et al. (1960), and Wittmann et al. (2007)
Pleasantly experienced symptoms of ego disintegration	Depersonalization, derealization, euphoria, emotional excitation, sense of unity.	Griffiths et al. (2011, 2006), Gouzoulis-Mayfrank, Thelen, et al. (1999), Hasler et al. (2004), Vollenweider et al. (2007, 1997, 1998, 1999), and Wittmann et al. (2007)
	Mania-like experiences with excitation and agitation (suggesting serotonin syndrome) were reported by some subjects.	Griffiths et al. (2006), Grob et al. (2011), Malitz et al. (1960), Rinkel, Dimascio, Robey, and Atwell (1961), Vollenweider (2001)

Continued

TABLE 4 Psychological Schizophrenia-Like Effects of Psilocybin—cont'd

Category of Symptoms	Symptoms	References
Negatively experienced symptoms of ego disintegration	Psilocybin induces psychological effects like anxiety, irritability, mood lability, primitive emotionality and emotional blunting.	Griffiths et al. (2006), Hasler et al. (2004), and Vollenweider et al. (2007, 1997, 1999)
	Progressing ego disintegration leads to thought disorder, loss of control on the content of thoughts, dysphoria, paranoid thinking, and panic-like attacks.	Gouzoulis-Mayfrank, Thelen, et al. (1999), Hasler et al. (2004), Malitz et al. (1960), Muscha et al. (1986), Penden et al. (1981), and Vollenweider et al. (1997)
	Impairment of coordination, behavioral slowdown, passiveness, and motor retardation or even complete inability to move were observed in some subjects. These effects on motor activity are supposed to be dependent on individual personality pattern.	Malitz et al. (1960), Rinkel et al. (1961), and Witmann et al. (2007)
	Voluntary performance of motor tasks like handwriting is impaired under hallucinogenic action of psilocybin, dependently on individual personality pattern.	Fisher, Kappeler, Wisecup, and Thatcher (1969)
	Passiveness and motor retardation also characterize depersonalization phenomena and loss of ego boundaries in psychiatric patients. Both excitement and stupor are commonly observed in certain types of schizophrenia (catatonic schizophrenia in particular).	Brauer, Harrow, and Tucker (1970) and Lerner et al. (1985)
Impairments of cognition and intellectual functioning	Cognitive functions are impaired in the course of intoxication, mainly working memory and attention ability.	Carter et al. (2005), Gouzoulis-Mayfrank et al. (2002), Hasler et al. (2004), Vollenweider et al. (2007, 1998), and Wittmann et al. (2007)
	Intoxicated subjects generally have difficulties in organization and verbalization of thoughts or are even unable to speak.	Malitz et al. (1960), Metzner et al. (1965), and Muscha et al. (1986)
	Psychometric measurements of the ability to solve simple mathematical problems revealed certain cognitive deficits and lower motivation.	Hollister (1961)
	Psilocybin induces impairment of manual skills, for example, it dramatically changes handwriting to become more awkward.	Fisher et al. (1969)
Schizophrenia-like information processing and symptoms of insufficient sensory gating	Psilocybin impairs prepulse inhibition of startle response to acoustic stimuli.	Vollenweider et al. (2007)
	Psilocybin does not affect auditory event-related potential mismatch negativity.	Umbricht et al. (2003)
	Early studies revealed that speech and thought content become disorganized and characterized with loosening of associations during psilocybin intoxication.	Malitz et al. (1960)
	Psilocybin promotes primary process thinking even at relatively low doses (0.08–0.2 mg/kg).	Martindale and Fischer (1977)
	The drug influences information processing, which could be demonstrated in an "AX"-type performance test.	Umbricht et al. (2003)
	At doses of 20 mg semantic priming was promoted.	Spitzer et al. (1996)

Symptoms of psilocybin-induced psychosis are grouped into several categories, including perceptual changes, symptoms of ego disintegration, cognitive deficits, and improper processing of contextual information.

Reported anxiety and fear of death partly originate from physiological side effects such as increased pressure and heart rate (Griffiths et al., 2011, 2006; Hasler et al., 2004). The symptoms result from an increase in unmetabolized catecholamines because psilocin stimulates the sympathetic system, adrenal medulla, and hypothalamopituitary–adrenal axis and competes with catecholamines as a substrate for monoamine oxidase (MAO). Some more experienced users have tried to combine psilocybin with MAO inhibitors. Psilocybin-induced cardiovascular complications were reported (Ghuran & Nolan, 2000). Emotionally evoked or stress-induced cardiovascular symptoms (pains, stinging) are sometimes anecdotally treated as indicators of remorse. Therefore, if produced in the course of

psilocybin intoxication, they could enhance religiousness and fear of death in less educated, more susceptible to suggestion individuals. Psilocybin-evoked endocrine effects are increases in adrenocorticotropic hormone, prolactin, thyroid-stimulating hormone, and cortisol (Gouzoulis-Mayfrank, Thelen, et al., 1999; Hasler et al., 2004). Transient elevation of thyroid-stimulating hormone may be coinvolved in euphoric effects and sexual arousal observed in some neurotic patients (Delay et al., 1963).

Psilocybin at relatively high doses induces effects described as mystical-type experiences, particularly in religiously inclined healthy subjects (Doblin, 1991; Griffiths et al., 2011, 2008, 2006; Leary et al., 1963; MacLean et al., 2011; Metzner et al., 1965). Some findings of the research, which prove the potential of psilocybin to produce negative emotions, are summarized in Table 5. Two dimensions of the Altered States of Consciousness Scale that measure symptoms of ego disintegration, namely oceanic boundlessness (assessing euphoria associated with depersonalization and derealization) and anxious ego dissolution (measuring disorder of thoughts, loss of self-control, and anxiety) are both highly sensitive to psilocybin (Gouzoulis-Mayfrank, Thelen, et al., 1999; Griffiths et al., 2011, 2006; Hasler et al., 2004; Vollenweider et al., 1998). Measures of mystical experiences based on classical modern psychology of religion incorporate negative emotions in the domain of sense of sacredness; psilocybin facilitates this category of experiences as well (Griffiths et al., 2011, 2006). It is worth mentioning here the reported psilocybin effects observed after collective ingestion, because in corporatized religious groups ego disintegration is a goal and the well-being of an individual depends on a sense of connection to a community (therefore exclusion from the community may be considered a punishment or a torture, and is practiced to maintain the group integrity or to manipulate the collective emotionality). In subjective reception psilocybin produces an illusionary transient sense of unity (Griffiths et al., 2011, 2006). However, collective ingestion does not enhance this effect. Metzner et al. (1965) demonstrated that highly subjective hallucinogenic effects occurred less often in cases of collective drug sessions. According to the authors, such experimental setting may produce a depressive mood or even aggression, despite positive expectations (Metzner et al., 1965). Similarly Leary et al. (1963) observed that in larger groups the drug session was experienced more negatively.

TABLE 5 The Main Findings of Studies Reporting Psilocybin-Induced Unpleasant Experiences of Mystical Type

Good Friday experiment by Pahnke (1962) (Doblin, 1991)	
Psilocybin dose	30 mg, nicotinic acid was used as active placebo
Participants	20 Protestant students of theology; the participants were divided into 10 groups of closely matched pairs based on previous psychological and physical tests, and one of the two received psilocybin, whereas the other was administered placebo.
Setting	Psilocybin was administered in a church during Good Friday service lasting 2.5 h; the chapel was decorated with typical religious symbols and equipment.
Sources of data	Questionnaire designed specifically for the experiment measured: sense of unity, transcendence of time and space, sense of sacredness, sense of objective reality, deeply felt positive mood, ineffability, paradoxicality, and transiency. Questionnaires were filled out 1 or 2 days after the drug session and half a year later; the participants prepared descriptions of their experiences shortly after the drug session and were interviewed shortly after the experiment and 6 months later.
Psychological and physiological effects that could contribute to unpleasant experiences and ego death phenomenon	Subjects reported anxiety, vivid imagery, sometimes frightening body image distortions. Mystical-type experiences were reported (all scores of all categories were higher in the psilocybin group than in the placebo group, 4 of 10 participants met criteria of complete mystical experience).
Leary et al. (1963)	
Psilocybin dose	Participants could choose the dosage by themselves. Range between 10 and 100 mg was available. The most frequent dosages were 12 and 20 mg. Writers had a tendency to choose the highest doses. Experiences interpreted as of mystical type were reported after a dosage of 30–40 mg.
Participants	175 volunteers participated in the study; they were mostly educated members of the middle class (graduate students, artists, writers, musicians, psychologists, housewives), but also some were prisoners.
Setting	Drug sessions were carried out in groups. A homelike environment was arranged. Participants were informed about possible drug effects prior to the drug session.
Sources of data	Subjects were asked to fill out a questionnaire and to write in their own words a report describing their experiences after the drug session.
Psychological and physiological effects that could contribute to unpleasant experiences and ego death phenomenon	Participants who ingested large doses (30 mg or more) tended to intellectually process their rather negative psilocybin-induced experiences (and possibly also other previous experiences) toward generalizations concerning unity with other people, hostility of other people, love, and faith in love. These literary descriptions could be interpreted as religious in essence. It was found that collective ingestion in larger groups tended to be experienced less pleasantly, more anxiously, and more personally.

Continued

TABLE 5 The Main Findings of Studies Reporting Psilocybin-Induced Unpleasant Experiences of Mystical Type—cont'd

Metzner et al. (1965)	
Psilocybin dose	Participants could choose the dose, the mean dosage was 0.59 mg/kg (25–30 mg).
Participants	82 volunteers, mostly (59%) psilocybin naïve, participated in the study. Among them were prisoners (26), graduate students (25), university teachers (4), and others (27). The experiments were carried out in groups.
Setting	Nonprisoners were administered psilocybin in homelike surroundings, prisoner sessions were conducted in a large hospital room.
Sources of data	Predrug and postsession measures of mood (Mood Adjective Check List); questionnaires to assess the subject's psychological state before the drug ingestion; a list of 108 content items grouped in 12 categories covering all possible effects, including physical symptoms and alternations of visual perception and cognition. These descriptions of potential effects could be accepted or rejected by participants in a graded manner.
Psychological and physiological effects that could contribute to unpleasant experiences and ego death phenomenon	Among the items increasing in frequency of reporting with dosage were emotions expressing helplessness and loss of control. Among the items most frequently accepted by the participants were those indicating primary process thinking. Younger subjects more frequently reported negative interpersonal experiences (isolation). Paranoid thinking and feelings of disintegration were reported by subjects who were preoccupied with problems at the time of the drug session or were anxious about the drug effects before the ingestion. Experiences of a mystical type were more frequently reported after higher doses and in cases in which subjects had previous experience with hallucinogens. However, items comprising religious-type emotionality expressed using literary phrases were among the most frequently rejected statements.
Griffiths et al. (2006)	
Psilocybin dose	30 mg/70 kg; methylphenidate 40 mg/70 kg was used as a control.
Participants	36 volunteers participated in the study, they were well-educated members of the middle class; around half of the group declared affiliation with a religious community, all declared some kind of involvement in religious activities, all were mentally healthy and had no previous experience with hallucinogens.
Setting	Homelike surroundings were arranged, during the drug session participants could listen to music and their eyes were covered with a mask to enhance occurrence of pseudo-hallucinations. They were observed by trained monitors during the session.
Sources of data	Blood pressure and heart rate were monitored at several time points during the drug session. Seven hours after the drug ingestion the subjects filled out questionnaires assessing subjective drug effects (Hallucinogen Rating Scale, Altered State of Consciousness Scale (APZ), Addiction Research Center Inventory) and mystical experiences (Oceanic Boundlessness of APZ Questionnaire, States of Consciousness Questionnaire, Mysticism Scale, Mysticism Scale—Lifetime). Before the drug experiment and 2 months later measures of psychiatric symptoms and personality traits were performed. Additionally, persisting effects were assessed (Persisting Effects Questionnaire). The participants were observed during the drug session. The sessions were also videotaped.
Psychological and physiological effects that could contribute to unpleasant experiences and ego death phenomenon	Increased blood pressure and heart rate were observed after psilocybin ingestion. No sedation was noted. According to ratings of the observers psilocybin elicited more stimulation and spontaneous motor activity, greater emotionality, and greater disconnection from common reality, with unresponsiveness to questions compared to methylphenidate. Nearly one-third of the participants (11 of 36) experienced fear during the psilocybin session, 8 of whom reported anxiety or dysphoria; six of the eight reported paranoid thinking. The total score and three derived factors of the Mysticism Scale were increased compared to the methylphenidate session (22 of 36 participants met criteria of complete mystical experience).
Griffiths et al. (2011)	
Psilocybin dose	0, 5, 10, 20, and 30 mg/70 kg, in an ascending or descending sequence; each participant had five sessions at 1-month intervals.
Participants	Eighteen hallucinogen naïve (except 1) volunteers participated in the study. They were well-educated members of the middle class, half of the participants declared affiliation with a religious community, all declared involvement in religious activities, all were mentally and physically healthy with no family history of psychotic disorders or bipolar disorder.

TABLE 5 The Main Findings of Studies Reporting Psilocybin-Induced Unpleasant Experiences of Mystical Type—cont'd

Setting	Eight-hour drug sessions were carried out in an aesthetic living room-like environment with two monitors present; during the drug session participants' eyes were covered with a mask to provide sensory deprivation facilitating production of pseudo-hallucinations.
Sources of data	Seven hours after psilocybin ingestion the participants filled out the following questionnaires: Hallucinogen Rating Scale, APZ, Addiction Research Center Inventory, States of Consciousness Questionnaire, Mysticism Scale (experience-specific). Cardiovascular parameters were monitored during the drug session. Persisting effects were assessed 1 and 14 months after the experiment based on questionnaires designed to measure the effects on attitudes, mood, behavior, and spiritual experience. Additionally poststudy ratings of persisting effects of the experiment were obtained from monitors and community observers.
Psychological and physiological effects that could contribute to unpleasant experiences and ego death phenomenon	Psilocybin produced significant dose- and time-dependent effects on cardiovascular parameters (heart rate, blood pressure). None of the subjects rated the experience as decreasing well-being; however, 7 of 18 reported fear and 5 of the 7 met criteria of complete mystical experience. Eight of 18 reported delusions or paranoid thinking; and 4 of the 8 met criteria of complete mystical experience.

Findings of the studies that considered psilocybin usefulness as an inducer of religious-type emotionality taking into account reported unpleasant experiences are summarized.

PSILOCYBIN-INDUCED COGNITIVE DEFICITS AND ITS ONEIROGENIC ACTIVITY

As already mentioned in the previous chapter psilocybin-treated individuals who met the criteria of a mystical-type experience (subjectively perceived mood improving with some features of delusional grandiosity and blurring of ego boundaries) after a single drug session became more intellectually active (MacLean et al., 2011). However, in terms of psychoanalysis mysticism usually is not considered a conceptual phenomenon and represents rather an example of regression to primary process thinking closely related to sensual bodily experiences (Cariola, 2012). If neurotoxin-induced experience is then conceptually processed and an individual undertakes efforts to support the resultant intellectual construct, it may be simply a form of defense mechanism (intellectualization, rationalization). Data from a brain metabolism imaging study suggest that certain defense mechanisms simplifying understanding of reality are likely to be triggered also directly under the action of psilocybin (Carhart-Harris, Erritzoe, et al., 2012; Gouzoulis-Mayfrank, Schreckenberger, et al., 1999). As seen in Table 4 psilocybin clearly affects cognitive functions. Cognitive challenge under the influence of psilocybin failed to activate prefrontal regions sufficiently (Gouzoulis-Mayfrank, Schreckenberger, et al., 1999). Deficits of attention ability and reduced arousal and vigilance are independent of 5-HT_{2A} receptor activation and probably result from 5-HT_{1A} inhibitory activity (Carter et al., 2005). It cannot be ruled out that some psilocybin/psilocin effects may result also from decreased blood flow and insufficient oxygen delivery (Carhart-Harris, Erritzoe, et al., 2012). Global elevation of brain glucose metabolism under the action of psilocybin was observed in a positron emission tomography study by Vollenweider et al. (1997). It should be mentioned here that imaging with fluorodeoxyglucose informs mainly about glucose uptake (increased in the case of insufficient oxygen delivery; nonoxidative glucose metabolism may be additionally impaired because fluorodeoxyglucose inhibits glycolysis). Psychedelic activity, particularly ego abnormalities, appeared associated with metabolic increases in the prefrontal cortex, the anterior cingulate, the temporomedial cortex, and the putamen (Vollenweider et al., 1997). Gouzoulis-Mayfrank et al. found correlates of the increased metabolic activity in the anterior cingulate with stereotyped thinking (positive) and with anxiety (negative) (Gouzoulis-Mayfrank, Schreckenberger, et al., 1999). Decreased metabolism in the left thalamus and in the composite bilateral subcortical region was associated with dysphoric reactions and fewer stereotyped thoughts (Gouzoulis-Mayfrank, Schreckenberger, et al., 1999). The alternations of blood flow directly observed by Carhart-Harris, Erritzoe, et al. (2012) were the most abundant in the thalamus, the anterior cingulate cortex, and the posterior cingulate cortex, which is a part of the default-mode network (DMN). Additionally functional connectivity studies revealed involvement of the DMN in the mind-altering effects of psilocybin (Carhart-Harris et al., 2013; Roseman, Leech, Feilding, Nutt, & Carhart-Harris, 2014). Psilocybin was also shown to decrease resting-state functional connectivity between the visual resting state networks and the sensorimotor network (Roseman et al., 2014). These effects may represent psilocybin-induced psychological regression related to ego blurring and the alternations of sensorimotor functions similar to the problems of early childhood.

Thus, under the action of psilocybin the thinking process is regressed and disorganized and, owing to semantic network spreading, may additionally become disturbed from paranoid delusions. Subjects are often at least partly aware of their cognitive incapability after psilocybin ingestion (Gouzoulis-Mayfrank, Schreckenberger, et al., 1999; Leary et al., 1963). In cases in which the subjects declare having mystical-type experiences, particularly those interpreted as introversive mysticism and of noetic quality, it may represent a certain type of helplessness related to cognitive deficits. Even if these alternations are transient, consciousness at moderate doses is usually not lost and all these unpleasant experiences may be kept in memory and may influence emotionality, personality, or view

of life. Some authors try to prove that even a single psilocybin experience may alter personality, although they are mostly concerned with the potentially positive impact of such experiences (Griffiths et al., 2008, 2006; MacLean et al., 2011). Conclusions in accordance with a definition of peak experience were made after careful application of a single dose (Griffiths et al., 2008, 2006; MacLean et al., 2011) because, as further studies revealed, repeated administration more negatively influenced the emotionality of the participants during intoxication, potentially increasing the probability of negative long-term side effects (Griffiths et al., 2011).

Psychedelic effects usually subside 5–6 h after oral administration of a pure compound, but when "magic mushrooms" are ingested the effects are delayed and the intoxication lasts longer. Accidental or intentional poisonings with mushrooms belonging to the genus *Psilocybe* have evoked psychotic reactions similar to delirium (Muscha, Ishii, Tanaka, & Kusano, 1986; Penden, Bissett, Macaulay, Crooks, & Pelosi, 1981). Perceptual alternations after ingestion of higher doses of pure psilocybin are also more similar to hypnagogic experiences, when normal waking consciousness and contact with reality are transiently lost (Griffiths et al., 2006). The oneirogenic activity of psilocin partly results from its action at 5-HT_{1A} inhibitory autoreceptors located on neurons of the dorsal raphe nucleus (Aghajanian & Marek, 1999). This activity may be very dangerous and even result in accidental death in recreational users—for example, strikingly often there are flying attempts or traffic accidents (Halpern & Sewell, 2005; Penden et al., 1981; Van Amsterdam, Opperhuizen, & van den Brink, 2011).

CONCLUDING REMARKS

In the previous chapter psilocybin was presented as an agent inducing peak experiences. Here we wanted to emphasize that psilocybin considered as an entheogen may produce euphoric experiences followed by an ego death phenomenon as well. Psilocybin has been used in spiritual healing ceremonies, was recommended as an adjuvant in psychotherapy, and is known to evoke schizophrenia-like psychosis. Thus, psychotherapy or religious practices supported with hallucinogens may increase the risk of serious mental disease. Depressive patients should be exposed very carefully to drugs interacting with 5-HT receptors because the periventricular system containing elements of the punishment circuit is responsive to serotonin. Modern societies are already exposed to psychoactive and addictive drugs, namely nicotine and alcohol. Attempts to propagate the legal usage of other psychoactive substances for religious or medicinal purposes in modern societies and among adolescents are alarming. Popularization of the described indolealkylamine as a substance that has been known and used for thousands of years may excessively encourage the abuse of magic mushrooms.

APPLICATIONS TO OTHER ADDICTIONS AND SUBSTANCE MISUSE

Psilocybin-induced hallucinatory experiences resemble anecdotal near-death experiences associated with states of hypoxia or ischemia, described rarely in scientific literature. The neurochemistry of sensations the survivors experience, may be analogous to the mechanisms of the stress-induced physiological fight-or-flight response and protective rearrangement within the pool of *N*-methyl-D-aspartate receptors (NMDA-Rs), preventing glutamate excitotoxicity. Similar phenomena are typical of ibogaine intoxication (Strubelt & Maas, 2008). The chemical structure of this compound is similar to both indolealkylamines and β-carbolines and reveals activities typical of these two classes of alkaloids (ibogaine is both a 5-HT_2 agonist and a MAO inhibitor). Combination of these two activities is practiced by Amazonian shamans who inebriate themselves with ayahuasca containing hallucinogenic substituted tryptamines and β-carbolines. However, ibogaine hallucinogenic and dissociative activity results mainly from the ability to inhibit NMDA-Rs. Ibogaine displays several other important activities; its pharmacodynamics is extremely complex, and intoxication may result in fatal cardiovascular complications. Psilocybin is also a vasoactive compound and may induce vasoconstriction manifested by peripheral cyanosis, it is effective in the treatment of cluster headaches or migraines, but it also means cardiotoxicity, particularly if coronary arteries are diseased, and subsequent hypoxia (Ghuran & Nolan, 2000). Serotonin syndrome and subsequent hyponatremia due to antidiuretic hormone elevation may develop in the course of psilocybin intoxication, particularly if combined with MAO inhibitors (including β-carbolines produced after alcohol consumption and present in tobacco smoke). Both are life-threatening conditions manifested by altered states of consciousness.

Thus, the symptomatology of near-death experiences is strikingly similar to that of hallucinatory states evoked with certain entheogens, including psilocybin. It seems like the psychoanalytic concept of a death drive, rather elusive and never formulated precisely since inspired by the natural sciences, although now out of date, is still present in both religious practices, containing aspects of archaic shamanism, and the more modern phenomenon of recreational drug abuse.

DEFINITION OF TERMS

Dysphoria This is an emotion opposite to euphoria and characterized by discomfort, anxiety, and dissatisfaction.

Ego death This is an unpleasant emotional phenomenon that follows signs of ego disintegration (depersonalization and derealization) and subsequent illusionary sense of unity, often associated with euphoria and delusions of grandiosity, enhanced with cognitive deficits.

Entheogen This is any psychoactive substance (usually of herbal origin) able to induce unusual effects, typically visual or emotional, applicable to religious teaching.

Id This is the unconscious part of personality containing primitive instinctual drives.

Mesolimbic pathway This is the dopaminergic pathway activated in response to rewarding stimuli (begins in the ventral tegmental area and connects to the nucleus accumbens via the medial forebrain bundle).

Pavlovian conditioning This is a type of associative learning in which an initially neutral stimulus is paired with another stimulus able to evoke an instinctive response and acquires the capacity to evoke this response when present alone.

Periventricular system This contains the brain structures (the hypothalamus, the thalamus, and the periventricular gray matter) involved in the punishment circuit.

Prison subculture This refers to the culture of prison society consisting of common values, beliefs, strictly obeyed rules, and rigid behavioral norms of ritual provenance, generally characterized by fatalism and pessimism, which support a social hierarchical structure with elements of slavery.

Semantic priming This is enhancement of recognition of a word if the word is preceded by a semantically related term.

Superego This is the structural part of personality reflecting learned moral standards.

KEY FACTS OF SCIENTIFIC INTEREST ON PSILOCYBIN AS AN ADJUVANT IN PSYCHOTHERAPY AND RELIGIOUS PRACTICES

- In 1939 an American anthropologist, Jean Basset Johnson, published an article describing ritual inebriation with magic mushrooms practiced by Mexican Mazatecs.
- In the early 1960s Hanscarl Leuner, the author of principles of psycholytic therapy, incorporated psilocybin into his therapeutic practice.
- Early studies on psilocybin conducted by Harvard psychologists led to psilocybin prohibition under U.S. federal criminal law in 1968.
- Scientific interest in psilocybin-induced experimental psychosis resumed in Switzerland at the end of the twentieth century.
- Studies conducted in the United States are focused more on religious-type emotionality induced by the drug.
- The research of British scientists on psilocybin's effects concerns the drug-induced changes in connectivity between brain structures forming functional networks.

SUMMARY POINTS

- The most pronounced effects of psilocybin are alternations of visual perception.
- Despite initial euphoria, the subsequent impairment of cognitive functions, schizophrenia-like symptoms of psychological regression, and spreading of the semantic network may negatively influence the content of thoughts or the displaying imagery.
- In particular, dysphoric reactions, paranoid thinking, anxiety, fear, or even panic attacks may develop in the course of intoxication.
- The alternations of perception and affect, identical to schizophrenia-like psychosis, may be interpreted religiously, and they enhance the development of the idea of God understood as a perfect and powerful being with certain attributes of fatherhood.
- The positive impact of such experiences on quality of personal or social life is doubtful.
- Exposure to psilocybin within hierarchically structured religious communities may increase already present tendencies toward psychological, sexual, and economical abuse of the worshipers.

REFERENCES

Aghajanian, G. K., & Marek, G. J. (1999). Serotonin and hallucinogens. *Neuropsychopharmacology*, *21*, 16S–23S.

Barabasz, A., Hyrnik, J., Janas-Kozik, M., & Jelonek, I. (2012). Faith vs. science: soul's possession or dissociative disorder? A case study. *Psychiatria Polska*, *46*, 305–312.

Brauer, R., Harrow, M., & Tucker (1970). Depersonalization phenomena in psychiatric patients. *British Journal of Psychiatry*, *117*, 509–515.

Carhart-Harris, R. L., Erritzoe, D., Williams, T., Stone, J. M., Reed, L. J., Colasanti, A., … Nutt, D. J. (2012). Neural correlates of the psychedelic state as determined by fMRI studies with psilocybin. *Proceedings of the National Academy of Sciences of the United States of America*, *109*, 2138–2143.

Carhart-Harris, R. L., Leech, R., Erritzoe, D., Williams, T. M., Stone, J. M., Evans, J., … Nutt, D. J. (2013). Functional connectivity measures after psilocybin inform a novel hypothesis of early psychosis. *Schizophrenia Bulletin*, *39*, 1343–1351.

Carhart-Harris, R. L., Leech, R., Williams, T. M., Erritzoe, D., Abbasi, N., Bargiotas, T., … Nutt, D. J. (2012). Implications for psychedelic-assisted psychotherapy: functional magnetic resonance imaging study with psilocybin. *British Journal of Psychiatry*, *200*, 238–244.

Cariola, L. A. (2012). A case study of primordial thought language and body boundary imagery in discourses of religious-mystical and psychotic altered states of consciousness. *ETC - Empirical Text and Culture Research*, *5*, 36–61.

Carter, O. L., Burr, D. C., Pettigrew, J. D., Wallis, G. M., Hasler, F., & Vollenweider, F. X. (2005). Using psilocybin to investigate the relationship between attention, working memory, and the serotonin 1A and 2A receptors. *Journal of Cognitive Neuroscience*, *17*, 1497–1508.

Chen, C. K., Lin, S. K., Sham, P. C., Ball, D., Loh, El.-W., & Murray, R. M. (2005). Morbid risk for psychiatric disorder among the relatives of methamphetamine users with and without psychosis. *American Journal of Medical Genetics, Part B, Neuropsychiatric Genetics*, *136B*, 87–91.

Ciccarone, D. (2011). Stimulant abuse: pharmacology, cocaine, methamphetamine, treatment, attempts at pharmacotherapy. *Primary Care: Clinics in Office Practice*, *38*, 41–58.

Ciprian-Ollivier, J., & Cetkovich-Bakmas, M. G. (1997). Altered consciousness states and endogenous psychoses: a common molecular pathway. *Schizophrenia Research*, *28*, 257–265.

Dein, S., & Littlewood, R. (2011). Religion and psychosis: a common evolutionary trajectory? *Transcultural Psychiatry*, *48*, 318–335.

Delay, J., Pichot, P., & Lemperierie, T. (1963). The therapeutic implications of psilocybine. In R. Crocket, R. A. Sandison, & A. Walk (Eds.), *Hallucinogenic drugs and their psychotherapeutic use Proceedings of the quarterly meeting of the Royal Medico-Psychological Association in London 1961:* (pp. 37–41). London: H.K. Lewis.

Doblin, R. (1991). Pahnke's "Good Friday Experiment": a long-term follow-up and methodological critique. *Journal of Transpersonal Psychology*, *23*, 1–28.

Fisher, R., Kappeler, T., Wisecup, P., & Thatcher, K. (1969). Measurement of handwriting area to pressure ratios during psylocybin-induced hallucinations. *Swiss Journal of Pharmacology*, *1*, 42–52.

Ghuran, A., & Nolan, J. (2000). Recreational drug misuse: issues for the cardiologist. *Heart*, *83*, 627–633.

Gouzoulis-Mayfrank, E., Hermle, L., Thelen, B., & Sass, H. (1998). History, rationale and potential of human experimental hallucinogenic drug research in psychiatry. *Pharmacopsychiatry*, *31*(Suppl. 2), 63–68.

Gouzoulis-Mayfrank, E., Schreckenberger, M., Sabri, O., Arning, C., Thelen, B., Spitzer, M., … Sass, H. (1999). Neurometabolic effects of psilocybin, 3,4-methylenedioxyethylamphetamine (MDE) and d-methamphetamine in healthy volunteers. A double-blind, placebo-controlled PET study with [18F]FDG. *Neuropsychopharmacology*, *20*, 565–581.

Gouzoulis-Mayfrank, E., Thelen, B., Habermeyer, E., Kunert, H. J., Kovar, K.-A., Lindenblatt, H., … Sass, H. (1999). Psychopathological, neuroendocrine and autonomic effects of 3,4-methylenedioxyethylamphetamine (MDE), psilocybin and *d*-methamphetamine in healthy volunteers. *Psychopharmacology*, *142*, 41–50.

Gouzoulis-Mayfrank, E., Thelen, B., Maier, S., Heekeren, K., Kovar, K. A., Sass, H., & Spitzer, M. (2002). Effects of the hallucinogen psilocybin on covert orienting of visual attention in humans. *Neuropsychobiology*, *45*, 205–212.

Griffiths, R. R., Johnson, M. W., Richards, W. A., Richards, B. D., McCann, U., & Jesse, R. (2011). Psilocybin occasioned mystical-type experiences: immediate and persisting dose-related effects. *Psychopharmacology*, *218*, 649–665.

Griffiths, R. R., Richards, W. A., Johnson, M. W., McCann, U., & Jesse, R. (2008). Mystical-type experiences occasioned by psilocybin mediate the attribution of personal meaning and spiritual significance 14 months later. *Journal of Psychopharmacology*, *22*, 621–632.

Griffiths, R. R., Richards, W. A., McCann, U., & Jesse, R. (2006). Psilocybin can occasion mystical type experiences having substantial and sustained personal meaning and spiritual significance. *Psychopharmacology*, *187*, 268–283.

Grob, C. S., Danforth, A. L., Chopra, G. S., Hagerty, M., McKay, C. R., Halberstadt, A. L., & Greer, G. R. (2011). Pilot study of psilocybin treatment for anxiety in patients with advanced-stage cancer. *Archives of General Psychiatry*, *68*, 71–78.

Halpern, J. H., & Pope, H. G., Jr. (2003). Hallucinogen persisting perception disorder: what do we know after 50 years? *Drug and Alcohol Dependence*, *69*, 109–119.

Halpern, J. H., & Sewell, R. A. (2005). Hallucinogenic botanicals of America: a growing need for focused drug education and research. *Life Sciences*, *78*, 519–526.

Hasler, F., Bourquin, D., Brenneisen, R., Bär, T., & Vollenweider, F. X. (1997). Determination of psilocin and 4-hydroxyindole-3-acetic acid in plasma by HPLC-ECD and pharmacokinetic profiles of oral and intravenous psilocybin in man. *Pharmaceutica Acta Helvetiae*, *72*, 175–184.

Hasler, F., Grimberg, U., Benz, M. A., Huber, T., & Vollenweider, F. X. (2004). Acute psychological and physiological effects of psilocybin in healthy humans: a double-blind, placebo-controlled dose-effect study. *Psychopharmacology (Berlin)*, *172*, 145–156.

Hollister, L. E. (1961). Clinical, biochemical and psychologic effects of psilocybin. *Archives Internationales de Pharmacadynamie et de Therapie*, *130*, 42–52.

Jablensky, A. (2010). The diagnostic concept of schizophrenia: its history, evolution, and future prospects. *Dialogues in Clinical Neuroscience*, *12*, 271–287.

Javitt, D. C. (2007). Glutamate and schizophrenia: phencyclidine, *N*-methyl-D-aspartate receptors, and dopamine-glutamate interactions. *International Review of Neurobiology*, *78*, 69–108.

Johns, A. (2001). Psychiatric effects of cannabis. *British Journal of Psychiatry*, *178*, 116–122.

Kapur, S. (2003). Psychosis as a state of aberrant salience: a framework linking biology, phenomenology, and pharmacology in schizophrenia. *American Journal of Psychiatry*, *160*, 13–23.

Kometer, M., Schmidt, A., Bachmann, R., Studerus, E., Seifritz, E., & Vollenweider, F. X. (2012). Psilocybin biases facial recognition, goal-directed behavior, and mood state toward positive relative to negative emotions through different serotonergic subreceptors. *Biological Psychiatry*, *72*, 898–906.

Krystal, J. H., Karper, L. P., Seibyl, J. P., Freeman, G. K., Delaney, R., Bremner, J. D., … Charney, D. S. (1994). Subanesthetic effects of the noncompetitive NMDA antagonist, ketamine, in humans. Psychotomimetic, perceptual, cognitive, and neuroendocrine responses. *Archives of General Psychiatry*, *51*, 199–214.

Leary, T., Litwin, G. H., & Metzner, R. (1963). Reactions to psilocybin administered in a supportive environment. *Journal of Nervous and Mental Diseases*, *137*, 561–573.

Lerner, H., Sugarman, A., & Barbour, C. G. (1985). Patterns of ego boundary disturbance in neurotic, borderline, and schizophrenic patients. *Psychoanalytic Psychology*, *2*, 47–66.

Leuner, H., & Holfeld, H. (1962). Results and problems of psychotherapy with adjuvant LSD-25 and related substances. *Psychiatria et Neurologia*, *143*, 379–391.

MacLean, K. A., Johnson, M. W., & Griffiths, R. R. (2011). Mystical experiences occasioned by the hallucinogen psilocybin lead to increases in the personality domain of openness. *Journal of Psychopharmacology*, *25*, 1453–1461.

Malitz, S., Esecover, H., Wilkens, B., & Hoch, P. H. (1960). Some observations on psilocybin, a new hallucinogen, in volunteer subjects. *Comprehensive Psychiatry*, *1*, 8–17.

Martindale, C., & Fischer, R. (1977). The effects of psilocybin on primary process content in language. *Confinia Psychiatrica*, *20*, 195–202.

Metzner, R., Litwin, G., & Weil, G. M. (1965). The relation of expectation and mood to psilocybin reactions: a questionnaire study. *The Psychedelic Review*, *5*, 3–39.

Muscha, M., Ishii, A., Tanaka, F., & Kusano, G. (1986). Poisoning by hallucinogenic mushroom hikageshibiretake (Psilocybe argentipes K. Yokoyama) indigenous to Japan. *Tohoku Journal of Experimental Medicine*, *148*, 73–78.

Naranjo, C. (1969). Psychotherapeutic possibilities of new fantasy-enhancing drugs. *Clinical Toxicology (Basel)*, *2*, 209–224.

Okahisa, Y., Ujike, H., Takaki, M., Mizuki, Y., Sakamoto, S., Mujun, W., … Uchitomi, Y. (2014). Association study of dopamine β-hydroxylase gene with methamphetamine psychosis. *Journal of Drug and Alcohol Research*, *3* Article ID 235792, 6 pages.

Penden, N. R., Bissett, A. F., Macaulay, K. E., Crooks, J., & Pelosi, A. J. (1981). Clinical toxicology of 'magic mushrooms' ingestion. *Postgraduate Medical Journal*, *57*, 543–545.

Rinkel, M., Dimascio, A., Robey, A., & Atwell, C. (1961). Personality patterns and reaction to psilocybine. *Neuro-Psychopharmacology*, *2*, 273–279.

Roseman, L., Leech, R., Feilding, A., Nutt, D. J., & Carhart-Harris, R. L. (2014). The effects of psilocybin and MDMA on between-network resting state functional connectivity in healthy volunteers. *Frontiers in Human Neuroscience*, *8*, 204.

Schmidt, A., Kometer, M., Bachmann, R., Seifritz, E., & Vollenweider, F. (2013). The NMDA antagonist ketamine and the 5-HT agonist psilocybin produce dissociable effects on structural encoding of emotional face expressions. *Psychopharmacology (Berlin)*, *225*, 227–239.

Spitzer, M., Thimm, M., Hermle, L., Holzmann, P., Kovar, K. A., Heimann, H., … Schneider, F. (1996). Increased activation of indirect semantic associations under psilocybin. *Biological Psychiatry*, *39*, 1055–1057.

Stockings, G. T. (1940). A clinical study of the mescaline psychosis, with special reference to the mechanism of the genesis of schizophrenic and other psychotic states. *Journal of Mental Science*, *86*, 29–47.

Strubelt, S., & Maas, U. (2008). The near-death experience: a cerebellar method to protect body and soul-lessons from the Iboga healing ceremony in Gabon. *Alternative Therapies in Health and Medicine*, *14*, 30–34.

Studerus, E., Gamma, A., Kometer, M., & Vollenweider, F. X. (2012). Prediction of psilocybin response in healthy volunteers. *PLoS One*, *7*, e30800. http://dx.doi.org/10.1371/journal.pone.0030800.

Trémeau, F. (2006). A review of emotion deficits in schizophrenia. *Dialogues in Clinical Neuroscience*, *8*, 59–70.

Umbricht, D., Vollenweider, F. X., Schmid, L., Grübel, C., Skrabo, A., Huber, T., & Koller, R. (2003). Effects of the 5-HT_{2A} agonist psilocybin on mismatch negativity generation and AX-continuous performance task: implications for the neuropharmacology of cognitive deficits in schizophrenia. *Neuropsychopharmacology*, *28*, 170–181.

Van Amsterdam, J., Opperhuizen, A., & van den Brink, W. (2011). Harm potential of magic mushroom use: a review. *Regulatory Toxicology and Pharmacology*, *59*, 423–429.

Van Os, J. (2009). "Salience syndrome" replaces "schizophrenia" in DSM-V and ICD-11: psychiatry's evidence based entry into the 21st century? *Acta Psychiatrica Scandinavica*, *120*, 363–372.

Vollenweider, F. X. (2001). Brain mechanisms of hallucinogens and entactogens. *Dialogues in Clinical Neuroscience*, *3*, 265–279.

Vollenweider, F. X., Csomor, P. A., Knappe, B., Geyer, M. A., & Quednow, B. B. (2007). The effects of the preferential 5-HT_{2A} agonist psilocybin on prepulse inhibition of startle in healthy human volunteers depend on interstimulus interval. *Neuropsychopharmacology*, *32*, 1876–1887.

Vollenweider, F. X., Leenders, K. L., Scharfetter, C., Maguire, P., Stadelmann, O., & Angst, J. (1997). Positron emission tomography and fluorodeoxyglucose studies of metabolic hyperfrontality and psychopathology in the psilocybin model of psychosis. *Neuropsychopharmacology*, *6*, 357–372.

Vollenweider, F. X., Vollenweider-Scherpenhuyzen, M. F., Bäbler, A., Vogel, H., & Hell, D. (1998). Psilocybin induces schizophrenia-like psychosis in humans via a serotonin-2 agonist action. *Neuroreport*, *9*, 3897–3902.

Vollenweider, F. X., Vontobel, P., Hell, D., & Leenders, K. L. (1999). 5-HT modulation of dopamine release in basal ganglia in psilocybin-induced psychosis in man–a PET study with [11C]raclopride. *Neuropsychopharmacology*, *20*, 424–433.

Wasson, R. G. (May 13, 1957). Seeking the magic mushroom. *Life Magazine*, *49*(19), 100–120.

Wigman, J. T., Vollebergh, W. A., Raaijmakers, Q. A., Iedema, J., van Dorsselaer, S., Ormel, J., … van Os, J. (2011). The structure of the extended psychosis phenotype in early adolescence–a cross-sample replication. *Schizophrenia Bulletin*, *37*, 850–860.

Wittmann, M., Carter, O., Hasler, F., Cahn, B. R., Grimberg, U., Spring, P., … Vollenweider, F. X. (2007). Effects of psilocybin on time perception and temporal control of behaviour in humans. *Journal of Psychopharmacology*, *21*, 50–64.