

Experimental Psychosis Research and Schizophrenia—Similarities and Dissimilarities in Psychopathology

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Abstract The aim of experimental psychopathology is to delineate overlapping functional disorders of psychoneurobiologically-defined systems where a set of common symptoms may correspond to a variety of nosological entities. According to the vulnerability model of psychosis, experimental research needs to go beyond categories such as “schizophrenia”. Prospective studies of the effects of psychoactive substances in normal control subjects offer several methodological advantages over routine clinical reviews of schizophrenic patients, especially in terms of standardization. Carefully designed studies utilizing a model psychosis paradigm are a step toward symptom-oriented research. Combining psychological and neurobiological techniques, the experimental psychopathological approach can provide us with a valuable tool for psychiatric research.

Keywords Experimental psychopathology • Hallucinogen induced model psychosis • Altered state of consciousness • Ego-/self disturbance • Key functions of model psychosis • Psychotoxic basic syndrome

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1 Introduction

Most of the early research into experimental psychosis was performed based on the assumption that hallucinogen-induced altered states of consciousness (ASC) are similar to schizophrenia spectrum disorders and therefore could be used as a “model” for investigating psychosis-related phenomena (Geyer and Vollenweider 2008; Hermle et al. 1992b; Vollenweider 2008; Vollenweider and Geyer 2001). Clinical case studies suggest that hallucinogen-induced altered states of consciousness (ASC) and schizophrenia spectrum disorders share a set of common symptoms (Chapman 1966). However, there is only weak evidence to support the hypothesis that the mental phenomena characteristic of the hallucinogenic intoxication can also occur during the incipient and acute stages of schizophrenia (Gouzoulis-Mayfrank et al. 1998). The aim of experimental psychopathology is to delineate overlapping functional disorders of psychoneurobiologically defined systems where a set of common symptoms may correspond to a variety of nosological entities. Therefore, in this chapter, the authors will present evidence regarding the similarities and differences between the psychopathology of schizophrenia and of hallucinogen intoxication.

2 The Beginning of the Experimental Method in Psychiatry

The first systematic clinical investigations of the intoxication produced by mescaline were conducted at the Munich Psychiatric University Hospital. In 1913, Knauer administered 0.15–2 g mescaline subcutaneously to nine physicians (Knauer and Maloney 1913). Knauer was the first to notice that psychological factors can influence the hallucinogen intoxication, and he was able to observe that repeated administration of mescaline to the same test subject would sometimes result in very variable experiences. Although studies from that time period had a great heuristic value, they also suffered from several methodological weaknesses. For example, the experimental conditions were not standardized and scientists would use plant extracts of variable composition. In the 1920s, Kurt Beringer studied the effects of mescaline using a more systematic approach that included repeated tests in his subjects. Beringer was inspired by the German psychiatrist Emil Kraepelin, a pioneer in psychopharmacological research. For the first time, investigations of mescaline were conducted using a standardized design, subjects were given a fixed dose (400–600 mg) using a single route of administration (subcutaneous), and subjective experiences were assessed in great detail. The goal of these experiments was to characterize the range of psychopathological effects produced by mescaline in healthy subjects and to compare mescaline-induced symptoms with those known to occur in endogenous psychoses. Publication of Beringer's monograph *Der Meskalinrausch. Seine Geschichte und Erscheinungsweise* ["The mescaline inebriation. Its history and phenomenology"] in 1927 marked the culmination of mescaline research in Heidelberg. With his mescaline trials, Beringer believed he had found an artificial model of psychosis because the effects of mescaline were very similar to the symptoms of acute schizophreniform diseases.

What impressed Beringer the most was the close similarity between the effects of mescaline and the symptoms present during the incipient stage of schizophrenia. In particular, Beringer found that both conditions lead to a state characterized by extremely rich and intense subjective experiences, which were described as being highly significant by both the mescaline subjects and the schizophrenia patients. Beringer called these states *Primärerlebnis* ["primary experience"] and noted that they often have a brief duration and are distinct from other phases of the illness, which are typically characterized by the absence of positive symptoms and development of progressive mental deficits. According to Beringer, the most important symptoms of the primary experiences in the model psychoses and schizophrenia are disturbances of self-awareness, experiences of ego-fragmentation, abnormal affect, mystical states, and feelings of enlightenment and revelation (Beringer 1927).

In addition to focusing on the development of a comprehensive phenomenological description of the course of the mescaline intoxication, Beringer's investigations also attempted to define how personality influences the mescaline intoxication. According to his own statements, Beringer was not able to identify a clear relationship between personality factors and the response to mescaline. Beringer's principle aim was the

search for an underlying disturbance that was common to both endogenous and drug-induced psychoses. By contrasting the symptoms occurring during primary experiences with those seen during the chronic phase of schizophrenia, Beringer stressed that there were both qualitative and quantitative differences. Furthermore, Beringer found that these two conditions may occur independently of each other and without one influencing the course of the other. Therefore, he concluded that the primary experiences have a biological basis and were unique entity within incipient schizophrenic illness and during mescaline intoxication.

3 Classification of the Subjective Effects of Hallucinogens

The complex phenomenology of the intoxication induced by mescaline and other hallucinogenic drugs has hampered development of a standardized nomenclature to describe and classify their effects. Depending on the perspective of the investigator, hallucinogenic drugs have been called *phantastics* (Lewin 1927) or *eidetics* (Hellpach 1941) to emphasize the visual hallucinations produced by these drugs; *hallucinogens* to describe pseudohallucinatory perceptual effects (Hoffer et al. 1967); *psychotics* (Becker 1949) and *psychotomimetics* (Leuner 1962) to describe the similarities between the hallucinogen intoxication and the symptoms of incipient or acute schizophrenia; *psychedelics* (“mind-manifesting”) to describe the positive, beneficial effects produced by these drugs (Osmond 1957); and *psycholytics* to describe their therapeutically useful effects, such as their ability to facilitate access to repressed and unconscious spheres of personality (Sandison 1954).

4 The Common Nucleus of Hallucinogen-Induced Altered States of Consciousness

Despite their pharmacological heterogeneity, Ludwig found that all hallucinogens produce similar psychopathological syndromes that are characterized by a primary alteration of consciousness and by secondary changes in cognition, perception, and emotion (Ludwig 1966). Dittrich further elaborated on the common core dimensions of hallucinogen-induced states of consciousness (Dittrich 1996). Extending Ludwig’s work, Dittrich (1998) identified three core dimensions that are consistently affected by hallucinogens: (1) *oceanic boundlessness*, (2) *dread of ego-dissolution*, and (3) *visionary restructuralization* (Fig. 1). These three core dimensions can be reliably measured by the APZ (*außergewöhnliche psychische Zustände*) questionnaire, which assesses altered states of consciousness (ASC).

Oceanic boundlessness (OSE) refers to positively experienced depersonalization and derealization, positive emotions, feelings of unity, and mystical experiences. *Dread of ego-dissolution* (AIA) refers to negatively experienced derealization and depersonalization, cognitive disturbances, catatonia, paranoid ideation, and loss of

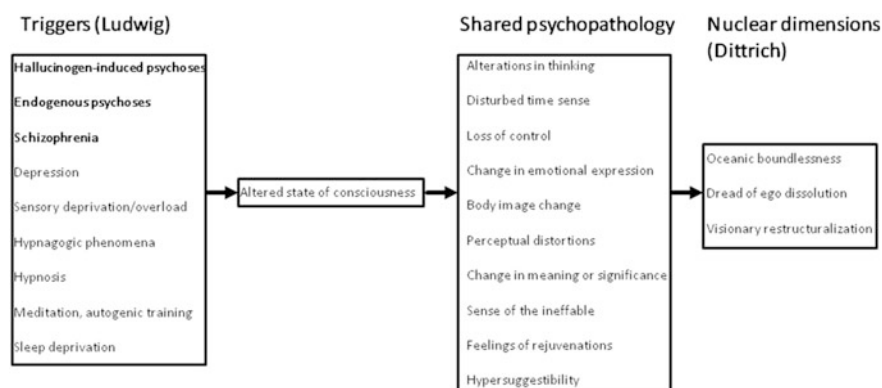


Fig. 1 The illustration shows that a variety of drug and non-drug conditions induce altered states of consciousness, leading to profound psychopathological changes. Altered states of consciousness consist of three core dimensions that have been found to be etiology-independent (Ludwig 1966; Dittrich 1996)

thought and body control; this indicates a very unpleasant state comparable to so-called bad trips. *Visionary restructuralization* (VR) refers to visual hallucinations, illusions, synesthesia, and changes in the meaning of perception. Vollenweider compared the effects of psilocybin ($n = 99$, 0.26 mg/kg p.o.), ketamine ($n = 68$, 0.012 mg/kg/min i.v.), and MDMA ($n = 74$, 1.5–1.7 mg/kg p.o.) on these three core dimensions in healthy volunteers (Vollenweider 2001). According to this comparison, both psilocybin and ketamine can produce ego-disintegration, an effect that is associated with either positive emotions or thought disorder and loss of self-control. Compared to psilocybin, however, *S-(+)*-ketamine and racemic ketamine produced higher levels of anxiety, thought disorder, and ego-disintegration. *S-(+)*-Ketamine and racemic ketamine also produced feelings of apathy, emotional withdrawal, and indifference—effects that are similar to the negative symptoms of schizophrenia. These findings support the contention that the effects of the dissociative anesthetics ketamine and PCP closely mimic the thought disturbances and cognitive deficits in schizophrenia (Table 1) (Krystal et al. 2000; Lahti et al. 2001; Vollenweider et al. 1997a, b, 1998b).

To determine whether the effects of hallucinogens are similar to the symptoms of endogenous psychosis, Gouzoulis-Mayfrank et al. (1998) compared 50 healthy controls, 93 patients with endogenous psychoses, and 7 hallucinogen-treated subjects using the APZ and a psychometrically improved version known as the OAV. The patients were examined after remission of their last psychotic episode and were directed to answer the two questionnaires with reference to the incipient phase of their psychotic disorder. Although there were significant differences between the scores of the psychotic patients and the healthy controls, there was little difference between the scores of patients with endogenous psychoses versus drug-treated subjects (Fig. 2). The results of this study support the hypothesis that there are phenomenological similarities between the experiences induced by hallucinogens

and the incipient stages of endogenous psychoses. The results also show that the OSE, AIA, and VUS dimensions of ASC are sensitive to the subjective phenomena that occur during acute episodes of schizophrenia. As noted by Gouzoulis-Mayfrank and co-workers, it is remarkable that schizophrenia episodes include experiences in the OSE dimension because in clinical practice it would be easier to overlook pleasant OSE experiences compared to negative experiences in the AIA dimension.

Following the tradition of Bleuler (Benedetti 1995), Döhmman asked 105 psychiatrists to assess whether any of the 158 items in the APZ reflect symptoms that are typically observed in patients with schizophrenia (Döhmman 1978). According to the psychiatrists, items from the AIA dimension were most consistent with the symptomatology of schizophrenia, indicating that the illness is often be associated with anxiety, derealization, and depersonalization. However, Döhmman did not focus on first-episode schizophrenia, which could potentially explain the preponderance of items from the AIA dimension. Schröter-Rosendahl assessed self-ratings of psychedelic experiences in 40 first-episode schizophrenia patients (Schröter-Rosendahl 1980). About 50% of the self-reports contained items from the OSE dimension, indicating that schizophrenic patients experience pleasant states in addition to anxiety. Visual perceptual changes (items in the VUS dimension) were rarely experienced by the patients, demonstrating that a robust difference exists between the effects of hallucinogens and the symptoms of schizophrenia.

5 Administration of Hallucinogens to Schizophrenia Patients

In the early 1930s, psychiatrists began to experiment with mescaline in schizophrenia patients in order to investigate whether subjects could distinguish the effects of hallucinogens from the symptoms of endogenous schizophrenia. Zucker (1930) administered mescaline to nine schizophrenia patients at doses between 350 and 400 mg. These trials confirmed that the patients could clearly differentiate mescaline-induced effects from illness-related hallucinations. Alternatively, various other clinicians (Kant 1930; Stockings 1940; Condrau 1949) believed the intoxications induced by mescaline, and LSD could serve as valid models of psychosis. For example, Condrau (1949) conducted a total of 197 experiments with LSD in 30 schizophrenic patients and found that the hallucinations induced by LSD were not discriminable from the patients' spontaneous hallucinatory symptom. Nevertheless, many clinicians had observed that schizophrenic patients were resistant to the effects of LSD and that individual reactions could vary substantially. Hoch (1957), for instance, found that patients suffering primarily from negative symptoms showed only minimal reactions compared to normal subjects, whereas schizophrenics with positive symptoms sometimes showed very intense reactions to mescaline and LSD.

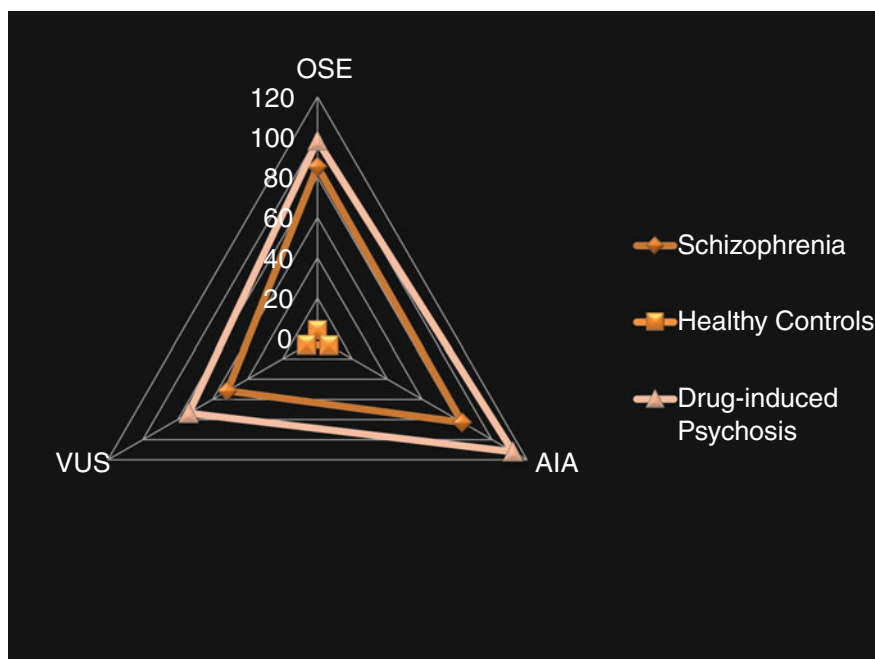


Fig. 2 Comparison of the scores on the three core dimensions of the altered states of consciousness scale (APZ) for schizophrenia patients ($n = 93$), healthy controls ($n = 50$), and hallucinogen intoxication ($n = 7$). Adapted from: Gouzoulis-Mayfrank et al. (1998)

Because there are now many schizophrenics who have used hallucinogens recreationally, comparing their experiences has provided important clues regarding the similarities and differences between the symptoms of schizophrenia and the effects of hallucinogen intoxication. Some patients report that their drug experience was completely different than their experience during the acute psychotic break. These results indicate that there are differences between the hallucinogen model psychosis and schizophrenia, but the difficulties associated with differential diagnosis and the high frequency of drug-induced schizophreniform psychoses argue for an overlap of pathogenesis. This is especially true if one assumes that a relatively non-specific mechanism is responsible for the development of schizophrenia. For example, according to the vulnerability stress model (Zubin and Spring 1977), only low doses of a hallucinogen would be required to induce psychotic reactions in susceptible individuals, making the old clinical dichotomy of provoked versus caused more of a continuum.

6 Similarities and Differences Between the Psychopathology of Psychosis and the Effects of Hallucinogens

6.1 Changes in Self-experience

The question of whether there is a close relationship between hallucinogen intoxication and endogenous psychosis—above and beyond their phenomenological similarities—is controversial and remains unresolved. The arguments for and against a common psychopathology will be summarized below for one specific disturbance: alterations of self-experience.

Self-awareness, also known as ego-consciousness, relates to the ability to conceive oneself as an individual, separate from others and from the environment, who can integrate and control their own thoughts, emotions, perceptions, and actions (Scharfetter 1995). Disorders of self-awareness, also known as self-disorders, comprise a variable set of symptoms and are nosologically unspecific, occurring in normal subjects after administration of hallucinogens as well as in patients suffering from schizophrenia, affective disorders, neurosis, or personality disorders. Self-disorders can also occur in healthy individuals, for example, during states of strong fatigue or of affective tension. There is substantial evidence that disrupted self-experience is a core disturbance of schizophrenia, which has been termed a self-disorder or an ipseity disturbance (*ipse* is Latin for “self”) (Sass and Parnas 2003). Bleuler, for example, noted that schizophrenia patients experience disruptions of the minimal sense of self, including splitting of their self-image, alterations of bodily experience, and loss of thought control (Bleuler 1911). Schneider (1955) was convinced that self-disorders due to schizophrenia and other causes should be discriminable; hence, he argued that the self-disorders in schizophrenia may have an important differential diagnostic value. By systematically studying self-experience in schizophrenic patients, Scharfetter (1995) identified five fundamental dimensions of self-consciousness that can reliably distinguish patients with schizophrenia from non-schizophrenic patients (e.g., patients with borderline personality disorder or depression):

1. *Ego-identity*—changes of one’s identity in respect to gestalt, physiognomy, gender, genealogy, and biography.
2. *Ego-demarcation*—loss of ego-boundaries and the ability to differentiate between self and non-self.
3. *Ego-consistency*—dissolution or destruction of a coherent, unified experience of the self, one’s thoughts, and the external world.
4. *Ego-activity*—altered ability to perform self-determined actions, thoughts, feelings, and perception.
5. *Ego-vitality*—fear of one’s death.

Table 1 Summary of the comparison of the dimensions of psychopathology during drug-induced hallucinations and schizophrenia (Vollenweider and Geyer 2001; Leuner 1962; Hollister 1961; Vollenweider 2001; Hermle et al. 1992a, b; Vollenweider et al. 1998a; Dumont et al. 2008)

	LSD, psilocybin, mescaline	Ketamine, PCP	MDMA	Amphetamine	Schizophrenia
<i>Ego-/self-dimensions</i>					
Ego-identity disturbance	+	+	?	(+)	+
Ego-demarcation disturbance	(+)	(+)	?	–	++
Ego-consistency disturbance	+	++	?	–	++
Ego-activity disturbance	+	++	?	(+)	+++
Ego-vitality disturbance	(+)	+	?	–	++
Reduction of reflecting self	+	++	?	–	+++
<i>Psychedelic core dimensions</i>					
Oceanic boundlessness	+++	+++	++	+	+++
Dread of ego-dissolution	+	++	(+)	+	+++
Visionary restructuralization	+++	++	+	(+)	(+)
<i>Symptoms</i>					
Visual hallucinations	+++	+(+)	–	–	+++ (acute) + (chronic)
Auditory hallucinations	(+)	(+)	–	–	+++
Delusions	(+)	(+)	–	–	+++
Negative symptoms	(+)	++	(+)	–	++

Mullen (2008) described experiences of passivity in schizophrenic patients, meaning they believed their internal mental processes were directed or influenced by outside forces or by other individuals. Beringer (1927) also wrote of a passivity syndrome in relation to the intoxication produced by mescaline. However, according to reports published by Arnold and Hoff (1953) and Weyl (1951), subjects using hallucinogens do not normally have the impression that their experiences are induced or controlled by outside forces. By contrast, Leuner (1962, p. 29), Savage (1955), and Grof (1967) noted that subjects treated with LSD and other hallucinogens sometimes believed their experiences were influenced or controlled by outside forces—in most cases, the investigators themselves or the investigational procedures.

To compare the changes of ego-functioning induced by drug intoxication and schizophrenia, Vollenweider and co-workers assessed first-episode schizophrenia patients as well as healthy volunteers administered psilocybin (15–20 mg p.o.), ketamine (0.02–0.03 mg/kg/min), or amphetamine (1.0 mg/kg p.o.) using Scharfetter's Ego Pathology Inventory (EPI) scale (Vollenweider et al. 1997a, b, 1998b; Vollenweider and Geyer 2001). At the doses studied, the dimensions *ego-identity* and *ego-consistency* were impaired to a similar degree in hallucinogen intoxication and schizophrenia. The dimensions of *ego-demarcation* and *ego-vitality*, however, were only slightly disrupted by hallucinogens while being severely impaired in schizophrenia (Table 1). Those authors concluded that the hallucinogen-induced model psychosis may be comparable to the symptoms of psychosis in schizophrenia patients, but with several important differences in the quality and quantity of effects on the ego-dimensions (Vollenweider and Geyer 2001). In particular, hallucinogen-treated subjects—unlike schizophrenic patients—typically recognized that their altered ego-functions were abnormal and retained insight into the fact that the changes were caused by a drug. The preservation of a residual self that is capable of reflection is the characteristic of hallucinogen effects and is only lost after administration of very high doses (Leuner 1962).

6.2 *Altered Body Experience and Depersonalization as Special Cases of Self-disturbance in the Model Psychosis*

There are numerous reports in the literature of altered body experience during hallucinogen intoxication (Beringer 1927; Arnold and Hoff 1953; Masters and Houston 2000; Savage and Cholden 1956; Heimann 1961; Stoll 1947). At the beginning of the mescaline intoxication, paresthesia-like sensations may occur, including sensations of vibration or electric shock, tingling, formication, and cold shivers (Beringer 1927). Moreover, there are reports of unpleasant muscular tension, feelings of heaviness in the limbs, and generalized muscle flaccidity. These so-called vegetative sensations appear to depend on the prevailing mood and personality of the subject (Hermle et al. 1992b). Alterations of body image may lead to disturbed self-experience and ego-dissolution. The dissolution of the boundary between the body and the outside world may be experienced as depersonalization phenomena (Stoll 1947). Body parts and even the entire body may be perceived as being separate from the self or may feel alien. Some subjects had out-of-body experiences where they felt that their consciousness was located outside of their physical body (Klee 1963; Hoffer et al. 1967; Savage 1955). It appears that these altered body experiences are often closely related to changes in perception or hallucinations. The perception of hallucinatory objects may lead to intensely experienced feelings that the self has merged with the cosmos and that the body has undergone a metamorphosis (Hermle et al. 1992b). Savage reported that bodily sensations during the hallucinogenic state may be intensely pleasurable (Savage and

Cholden 1956). Hence, the altered bodily experiences induced by hallucinogens have been described as both an intensification of the bodily self and a dissolution of the boundary between the body and the external world. Alterations of bodily experiences typically occur at the beginning of the intoxication and are paralleled by a more general change of self-experience where the drug state causes the subject to focus their attention inward (Heimann 1961).

6.3 Alteration of the Experience of Time and Space

Changes of the perception of three-dimensional space during the hallucinogen intoxication can vary widely. Objects seen may be perceived especially vividly, with increased differentiation of colors and brightness, as well as enhancement of stereoscopic vision (Beringer 1927, p. 39). Illusory motion and distortions of perspective, including micropsia, macropsia, and dysmegalopsia, are frequently reported (Beringer 1927, p. 43). In the context of these distortions of visual perception, the environment may be experienced as being abnormally large or threateningly small, and like the depersonalization experiences, the boundary between the body and the external world may be distorted. Alterations of the perception of time are frequently reported during hallucinogen intoxication (Beringer 1927; Becker 1949). Time is either perceived to be contracted, dilated, or the sense of time may completely dissolved. If the disturbed temporal experiences coincide with hallucinogen-induced euphoria, then they may lead to feelings of ecstatic exhilaration; alternatively, if accompanied by anxiety, the altered temporal experiences may intensify the negative feelings due to the impression that time has stopped (Becker 1949; Cohen 1968).

Changes in time perception have also been reported in patients with schizophrenia. For example, it has been shown that schizophrenic patients tend to overestimate elapsed time (Bonnot et al. 2011) or have less ability to judge correctly the temporal order of acoustic stimuli (Braus 2002).

6.4 Passivity Syndrome

Even some of the earliest studies noted that the hallucinogen intoxication can include elements of withdrawal and passivity that resemble the negative symptoms of schizophrenia (Hermle et al. 1992b). Some hallucinogen test subjects found themselves to be withdrawn and inactive, perceiving environmental stimuli in a passive and unfiltered manner, and at least partly incapable of controlling their thoughts, experiences, and behavior. At the peak of the mescaline intoxication, subjects may be so passive and inwardly focused on the experience that self-reflection or engagement with the external world is greatly reduced or impossible (Beringer 1927).

6.5 Self-loss

Self-loss refers to a very severe manifestation of self-disturbance. There may be feelings of loss of ownership of thoughts, perceptions, experiences, or emotions, or those things may feel alien in nature; additionally, the environment and time may no longer feel independent from the self or may completely cease to exist. These states are frequently accompanied by severe agitation and anxiety. Someone who takes a drug usually retains insight into the cause of the eventual changes, but those suffering from endogenous psychosis are not aware of the cause of their symptoms (Hermle et al. 1988). These responses appear to be an understandable reaction to changes of experiences that make the subject feel helpless. With further dose increases, an apocalyptic phase sets in (Conrad 1958, p. 104), which is characterized by loss of self-control and decay of the coherent self. As a consequence of these highly severe psychotic states, catatonic behavior may occur (Kraehenmann et al. 2010).

7 The Six Key Functions of the Model Psychosis Induced by Hallucinogens

In order to compare the phenomenology of schizophrenia and hallucinogen-induced experiences, Leuner (1962, p. 219) attempted to work out the key psychopathological features of the hallucinogen intoxication. Leuner regarded the so-called *psychotoxic basic syndrome* as the key functional substrate of the experiences produced by hallucinogens (Fig. 3). Importantly, there seems to be a uniform and consistent pattern of changes of psychological functioning that is common to all hallucinogenic substances. The *psychotoxic basic syndrome* is characterized by a regression of psychological functioning to ontogenetically earlier stages, as well as a shift from normal, waking consciousness to a so-called state of protopathic consciousness (Greek, proto-, “first, primitive” + pathos, “suffering, feeling”) (Lienert 1959; Conrad 1948; Lohmar and Brudzinska 2011). The *psychotoxic basic syndrome* is similar to the *hypnagogic basic syndrome*. It is characterized by spontaneous symbolic visual phenomena and intensified mood and affect that occurs during hypnosis, before falling asleep, and during sensory deprivation (Leuner 1962). In the protopathic state, abstract thinking is impaired and thoughts are easily transformed into imagery (Klee 1963).

According to Leuner (1962), hallucinogenic states progress over time according to two basic patterns: (1) a “fluctuating-scenic” or “quasi-normal” course, and (2) a “stagnating fragmentary” or “extreme psychotic” course. During the quasi-normal course, subjects experience a continuous flow of imagery, accompanied by a significant emotional response. This experience is very similar to dreaming. If the level of emotional arousal peaks, there may a dissociation between conscious experience and emotional response. In that situation, the scenic course of intoxication may be

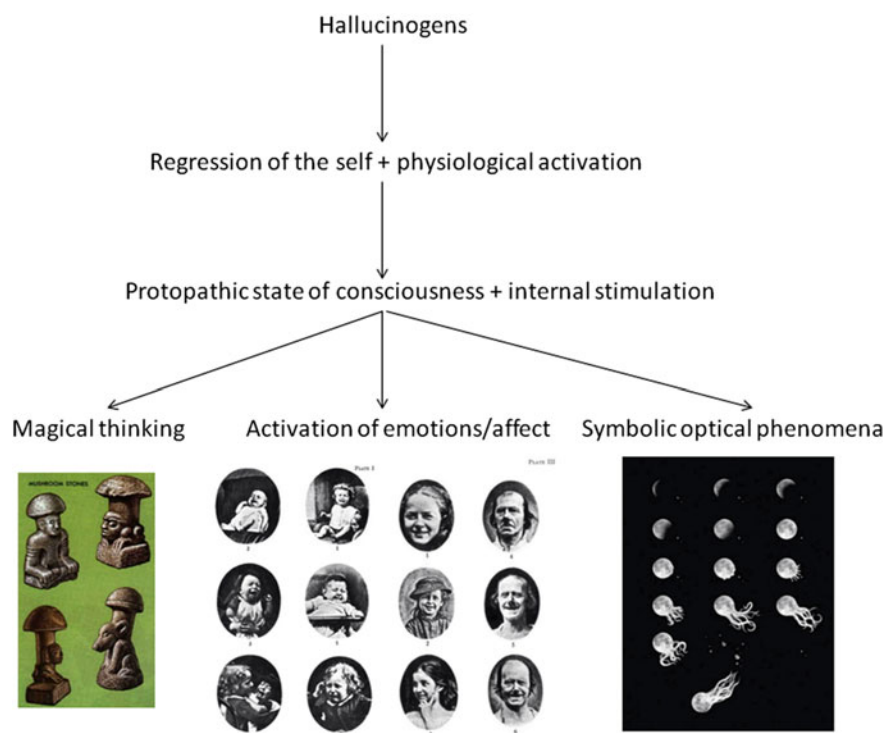


Fig. 3 Schematic illustration of the “psychotoxic basic syndrome” proposed by Leuner (1962) to explain the profound alterations of cognition, emotions, and perception produced by hallucinogens

interrupted and seemingly random fragmentary experiences may occur, often accompanied by inadequate affect and stereotypical motor behavior (a catatonic syndrome). Importantly, Leuner found that during an individual session, the hallucinogen intoxication may fluctuate between a quasi-normal course and an extreme psychotic course. Leuner also reported that even seemingly personality-neutral scenic visual hallucinations (e.g., images of animals, monsters, and mythical creatures) are often endowed with personal meaning. He categorized six key functions underlying the psychological effects of hallucinogens:

1. **Activation of intrapsychic processes:** On the one hand, hallucinogens activate physiological and psychological processes, including emotions and imagery; on the other hand, hallucinogens impair cognitive control; both effects lead to an enhancement of internally generated experiences;
2. **Dynamic overdrive of the psyche:** Mental hyperarousal and loss of control over thoughts and emotions further lead to a seemingly random succession of imagery, dissociation of affect, and motor reactions ranging from catatonia to hyperactivity;

3. **Transphenomenal dynamic governing system:** Individual memories are co-activated with associated thoughts and emotions, which can further drive and influence the hallucinogen experience and behavior;
4. **Dynamic reduction:** A gradual reduction of hyperarousal and dynamic overdrive in the course of time;
5. **Deep psychological affective dynamics:** expression of emotional themes via symbolic imagery, reliving of emotionally charged childhood memories, and cathartic abreaction; and
6. **Dynamic fixation:** The psychotic content of the experience is stagnant and fails to progress or change over time, potentially as a defense mechanism.

Therefore, Leuner revised Beringer's proposal that the experimental psychosis was not influenced by repressed material. Leuner found that it was even possible to identify symbolic content and repressed affective material during the course of extreme psychotic reactions (with catatonia and stupor), which is why it is possible to effectively perform psychotherapy in "psychotic" patients under the influence of hallucinogens.

8 Changes in Perception

Since the beginning of research into substances that mimic schizophrenia, it has been repeatedly discovered that hashish, mescaline, psilocybin, and LSD have a common effect: They intensify sensory perception and induce a wealth of subjective experiences (Beringer 1927; Leuner 1962; Stoll 1947; Joel and Fränkel 1926). The drug-induced alterations of perceptual processes can be categorized into three basic types (Boor 1956): (1) changes related to sensory input; (2) hallucinatory changes; and (3) alteration of the meaning of percepts. Changes related to sensory input (group 1) are characterized by only minimal alterations of their formal qualities (e.g., shape and color). Chromatopsia, micropsia, macropsia, and spatial distortions are examples of perceptual alterations belonging to this class. Hallucinations (group 2) are sensory perceptions that occur in the absence of external stimuli. Changes in the significance or meaning of sensory perceptions (group 3) are known to occur frequently in hallucinogen intoxication and incipient schizophrenia; these symptoms have been termed delusional perceptions. Delusional perception refers to the phenomenon where a patient believes that a normal percept has abnormal meaning, often with self-reference.

The degree to which the hallucinations and perceptual disturbances in schizophrenic patients overlap with the hallucinations induced by LSD and related substances has been addressed by several authors over the past few decades. It is believed that patients with schizophrenia primarily experience auditory hallucinations, whereas LSD-like drugs tend to cause visual hallucinations. These differences have frequently been cited as evidence that hallucinogen effects and schizophrenic symptomatology can be differentiated. However, others have noted that

hallucinogens can sometimes produce acoustic hallucinations and that some patients with schizophrenia experience severe visual hallucinations (Chapman 1966; Hoffer and Osmond 1966; Small et al. 1966; Freedman and Chapman 1973; Young 1974; Winters 1975). These authors emphasized that the acute phase of schizophrenia is often associated with perceptual disturbances that are very similar to drug-induced hallucinations. According to Chapman (1966), delusions that develop in schizophrenia patients often occur in response to specific perceptual disturbances, making it difficult to differentiate between their hallucinations, illusory misperceptions, and delusional perceptions. Further, it has been argued that the difference between drug-induced hallucinations and the hallucinations in schizophrenia may to some degree be dependent on time rather than the underlying illness. For example, Winters (1975) postulated that the temporal stages of schizophrenia may be understood in analogy to a chronic state of hallucinogen-induced intoxication, where the typical schizophrenic symptoms such as multisensory perceptual disturbances and delusional ideation follow the initial visual hallucinations.

The extent to which the evaluation of perceptual disturbances relating to syndrome genesis may influence the classification of model psychoses was made clear by Hoffer and Osmond (1966). The authors noted that psychiatrists tend to ignore perceptual disorders in patients with schizophrenia, which they theorized occurs because Bleuler believed that perception is unaltered in schizophrenia (Bleuler 1911). By contrast, Hoffer and Osmond suggested that perceptual disturbances are a common occurrence in schizophrenia patients and should be viewed as a primary illness process and not as a secondary response (Hoffer and Osmond 1966; also see Kraehenmann et al. 2012). Previously, Beringer (1927), Stockings (1940), and Savage and Cholden (1956) noted that hallucinogen-like visual alterations may occur in the early stages of spontaneous psychotic states, although they believed that such phenomena would be easily overlooked. According to Söllwold and Huber (1986) and Klosterkötter et al. (1994), these subjective visual alterations occur during the prodromal phase of psychosis. Before the start of an acute psychotic episode, the prodromal symptoms become more intense and are often accompanied by fluctuating affect; eventually, the prodromal symptoms progress to classical psychotic symptomatology, such as delusional phenomena.

9 Inter- and Intra-individual Differences

The personality structure of test subjects, as well as differences in the integration of self-related functioning and affective responses, often influences the symptoms of the intoxication induced by hallucinogens (Leuner 1962, p. 43; Linton and Langs 1962; Ziolkowski 1966, p. 250; Grof 1967, p. 160). For example, subjects with compulsively structured personalities exhibit weak responses to moderate doses of hallucinogens (Langs 1967, p. 182; Leuner 1962, p. 44; Buckman 1967). Alternatively, subjects with histrionically structured personalities are highly

sensitive to low doses of hallucinogens (Grof 1967, p. 161). Within individual subjects, there may also be substantial differences across test sessions (Sandison 1954; Leuner 1962, p. 446; Cohen 1968). Initially, test subjects are often disturbed by the vegetative symptoms produced by hallucinogens (e.g., hypertension, tachycardia, mydriasis, hyperthermia, tremor), but these symptoms often recede into the background. Likewise, the intensity of hallucinations, concentration deficits, and self-disturbances often gradually declines from session to session, giving way to well-arranged (so-called quasi-normal) experiences (Leuner 1962, p. 45). Leuner (1962, p. 45) described a “paradoxical habituation” where, after several hallucinogen experiments, test subjects would sometimes only need half the dose amount to be brought into an inebriation experience of similar intensity. The influence of *setting* appears to be of special importance here.

The effects of hallucinogens are extremely dose-dependent. Leuner (1962) divided hallucinogen effects into three dose ranges: At low doses (e.g., 25–80 µg LSD), hallucinogens tend to produce euphoria and a loosening of associations; medium doses (e.g., 80–200 µg LSD) produce a broad spectrum of psychopathological effects, including hallucinations and depersonalization; high doses (200–700 µg LSD) can provoke extreme disorientation, as well as loss of insight into the drug-induced nature of the experience, potentially resulting in extreme agitation or catatonia. The mystical experiences produced by hallucinogens are most likely to occur after administration of high doses.

10 Differential Typology of Intoxication and Psychosis

In the literature, the terms drug-induced intoxication and drug-induced psychosis are often used synonymously with regard to hallucinogen intake. Clarification of these terms, however, allows intoxications to be distinguished from psychoses. The terms *hallucinogen intoxication* and *hallucinogen-induced psychosis* are not uniformly defined and differentiated, which is a consequence of their very diverse psychopathological presentation. In order to define and evaluate these terms, it is necessary to understand the spectrum of effects produced by individual hallucinogens as well as the many factors that can influence the occurrence of intoxication and psychosis. Whereas intoxication may be directly traced back to the pharmacological effects of hallucinogens, a drug-induced psychosis can occur in the absence of recent hallucinogen use (ICD-10-CM: F16.9; F16.75).

11 Conclusions

Among psychiatrists, it is a widely held opinion that visual hallucinations predominate the hallucinogen intoxication, whereas auditory hallucinations predominate in schizophrenia. However, this view is not completely accurate, possibly due

to unclear terminology; many of the so-called visual hallucinations occurring in hallucinogen intoxication correspond to complex perceptual disturbances that can only be described verbally with great difficulty (Spitzer 1988). Diverse changes in visual perception can also occur in the beginning phases of schizophrenia, although these symptoms often go undetected because most psychiatrists focus on the acoustic hallucinations that occur later in the developmental course of schizophrenia. Between the model psychosis produced by hallucinogens and the acute state of schizophrenia, there appears to be no basic difference in terms of the psychopathological phenomena that can occur. Therefore, we believe that the term model psychosis is well deserved and may be used as a tool to study “endogenous” psychoses (Bowers and Freedman 1966).

Experiments using such models in healthy subjects offer many advantages compared to the spontaneously developing psychoses. One major advantage is the fact that in normal subjects brain function is not impaired by a preexisting illness process. In addition, the findings before, during, and after remission of the hallucinogen intoxication may be compared using within-subject measures. Using this technique, it is possible to avoid the difficulties associated with the existence of large inter-individual differences in biological and psychological variables in schizophrenia patients. The aim of research is the identification of so-called linking variables that connect clinical psychopathological phenomena with the underlying biological factors (Callaway 1992).

The aforementioned considerations make it clear that states of hallucinogen-induced intoxication are not a specific model for functional endogenous psychosis; due to the relatively short duration of hallucinogen intoxication, the effects may at best resemble the symptoms of incipient psychosis. Depending on the dose, set (i.e., individual vulnerability to the effects of hallucinogens), and setting, the hallucinogen intoxication corresponds to the prodromal phase of schizophrenia in the sense of the “trema” according to Conrad (1958) and the type of dynamic instability according to Janzarik (1959). Sometimes, a fully developed psychosis (in the sense of dynamic overdrive according to Leuner (1962) and the “apophenia” or “apocalypse” according to Conrad (1958)) may develop, which may present as a catatonic state. The etiopathogenetic mechanisms of functional psychoses and of the hallucinogenic inebriation may be different, but in view of a putative common psychopathological final pathway, one may assume a similarity in their underlying neurobiological mechanisms. Therefore, analogical conclusions from the so-called experimental psychosis to naturally beginning psychotic illness processes may be justified. By combining psychological and neurobiological techniques, the experimental psychopathological approach can provide us with a valuable tool for psychiatric research (Sessa 2005).

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