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Ceci n'est pas une psychose. Toward a Historical Epistemology of Model Psychoses

Nicolas Langlitz
Department of Anthropology, University of California, Berkeley, CA, USA
E-mail: langlitz@berkeley.edu

Abstract
After an interruption of almost 20 years, psychopharmacological research on hallucinogenic drugs was revived in several countries simultaneously around 1990. Most of the projects that have been initiated since then have been based on the conception of model psychosis: by administering hallucinogens to healthy test subjects, psychiatrists induce a state regarded as an artificial and temporary psychosis, which can be studied under controlled experimental conditions in the laboratory. As a model of psychosis, the hallucinogen intoxication is meant to provide important clues to schizophrenia research. This article examines the history of the concept and practice of model psychosis in order to demarcate the peculiarities of its most recent articulation in the vocabulary of cognitive neuroscience. It highlights the shift from phenomenological to biological psychiatry. The analysis contributes to an understanding of the 'regional epistemology' of psychopharmacology by reflecting on the question: what kind of a model is the hallucinogen model of psychosis?

Keywords Drugs, Hallucinogens, Models, Psychedelics, Psychopharmacology, Psychosis

After almost 20 years of relative calm following the turmoil around the uses and abuses of hallucinogenic drugs in the 1960s and 1970s, there has been a renaissance of hallucinogen research in psychiatry and psychopharmacology since about 1990. The renewed interest in this class of substances has taken a number of different forms, none of which is genuinely new. Certain actors took up the idea of using hallucinogens (or related entactogens like MDMA) to facilitate various forms of psychotherapy (e.g. Gasser, 1997; Sessa, 2005). Some conceived of such psychotherapeutic applications as (neo-) shamanic or quasi-religious rituals contributing to the spiritual health and well-being of their patients and clients (e.g. Bravo and Grob, 1989; Grob *et al.*, 1996). However, apart from these practices, employing hallucinogens as vehicles to an authentic self or profound spiritual truths, there has also been a psychiatric tradition, often at odds with these perspectives, in which the symptoms provoked by hallucinogens have been compared to the clinical picture of

Nicolas Langlitz studied medicine and philosophy in Berlin and Paris. He wrote a dissertation on the psychoanalyst Jacques Lacan's practice of variable-length sessions, which was published as *Die Zeit der Psychoanalyse: Lacan und das Problem der Sitzungsdauer* (Frankfurt/M.: Suhrkamp, 2005). At present, he is doing a PhD in Medical Anthropology at UC Berkeley and UC San Francisco. He is also an associated researcher of the Laboratory for the Anthropology of the Contemporary (www.anthropos-lab.net).

psychosis. As 'psychotomimetics', or psychosis-mimicking drugs, they have been used as research tools to examine psychotic states in healthy test subjects under controlled experimental conditions. Here, the hallucinogen intoxication is taken as a model of psychosis, particularly of schizophrenia. For political as well as scientific reasons, such model psychosis research has played a central role in the revival of hallucinogen research in recent years. The aim of this article is to demarcate the contemporary re-articulation of the model psychoses from previous forms.

For this purpose, I discuss the uses of hallucinogen models of psychosis in the twentieth and early twenty-first century. I cannot and do not wish to recount the complete history of this important chapter of the history of psychiatry.[1] Instead, I concentrate on two periods: Kurt Beringer's work on the mescaline model of psychosis in the 1920s and the most recent episode of model psychosis research beginning in the late 1980s. I analyze the changes in the underlying rationality brought about by the shift from phenomenological to biological psychiatry and address the question of what kind of model the hallucinogen model of psychosis is and how those working with it understand its epistemological status. In this respect, the limits of the model seem as important as the positive representational relations between the model and its object. After all, the differences perceived between schizophrenia and the effects of hallucinogens contribute as much to conceptions of this mental disease as the similarities. As it turns out, the current uses of hallucinogen models of psychosis primarily serve to produce questions, not answers to fuel schizophrenia research.

The approach pursued in this article can be described as a certain kind of historical epistemology. In his book *Models*, the philosopher of science Marx Wartofsky reprints an essay from 1973 entitled 'Perception, representation, and the forms of action: Towards an historical epistemology' (Wartofsky, 1979: 188–210). His basic argument is that we do not perceive the world passively, but mediated by representations, which we make. The kinds of representation featuring most prominently in Wartofsky's book are models. Being produced by human action they are subject to historical change. However, Wartofsky does not trace the transmutations of a single concrete model. His concept of model remains abstract and ahistorical. Ian Hacking proposed a 'historical meta-epistemology' to historicize such organizing concepts and practices that 'have to do with knowledge, belief, opinion, objectivity, detachment, argument, reason, rationality, evidence, even facts and truth' (Hacking, 2002: 8; see also Hacking, 1999). A historical meta-epistemology of models and modeling would allow taking Wartofsky's argument one step further. It is—to my knowledge—still a desideratum. In this article, however, I neither intend to provide an epistemological discussion of models in general (although Wartofsky's philosophical argument—ahistorical as it might be—contributes to my reading), nor do I aim at a metahistorical analysis of the 'organizing concept' of model.[2] Instead I will focus on the empirical concept and practice of the hallucinogen model of psychosis as an aspect of the 'regional epistemology' of psychopharmacology.

1 Much valuable work on the history of the hallucinogen models of psychosis has already been done by Vannini and Venturini (1999). Moreover, current model psychosis researchers have also written about the history of their field: Gouzoulis-Mayfrank *et al.* (1998b), Hermle *et al.* (1988, 1993).

2 For a brief history of the concept of model, see Kaulbach and Mainzer (1972).

Beringer's experiential model of psychosis

The idea of mimicking a mental disorder by administering a drug goes back to the French psychiatrist Jacques-Joseph Moreau de Tours. In the 1840s, he experimented with psychoactive substances, mostly with hashish, at the Hôpital de Bicêtre and in the Club de Haschischins in Paris. In his study *Du hachisch et d'aliénation mentale* (1845), Moreau described the effects of hashish on healthy subjects (among them poets such as Charles Baudelaire, Honoré de Balzac, Théophile Gautier and Gérard de Nerval as well as painters like Eugène Delacroix) (Healy, 2002: 180; Jay, 1999: 253; Plant, 1999: 72). He wrote: 'In the way in which it affects the mental faculties, hashish gives to whoever submits to its influence the power to study in himself the mental disorders that characterize insanity, or at least the intellectual modifications that are the beginning of all forms of mental illness' (quoted in Jay, 1999: 20). He wanted to make use of the consciousness-altering properties of the drug in order to allow physicians and artists to acquire personal insights into the 'lived experience' of psychopathological phenomena. However, Moreau's approach did not gain currency. As historian of psychopharmacology David Healy puts it: 'Despite the widespread use of a variety of consciousness-altering agents during the nineteenth century, Moreau's idea was too radical. It was a century before it was picked up again' (Healy, 1997: 113).

When the German psychiatrist Kurt Beringer took up Moreau's approach in 1921, he used the alkaloid mescaline, which had been isolated from the Mexican peyote cactus in 1896 and synthesized in 1919 by German chemists. Beringer proposed that mescaline intoxication could serve as a model of psychosis.[3] Beringer was also hoping that he could use mescaline as a probe to explore a subject's personality. He expected the contents of the psychotic experiences provoked by the drug to reveal something about a subject's individual constitution as well as his or her unconscious processes. Although he did find that the momentary psychological condition influenced the effects of the drug, he could not identify any stable relationship between the individuality of a certain person and his or her drug experiences (Beringer, 1927: 105). No inner truth came to the fore. Instead Beringer reported a variety of misperceptions of reality. Mescaline-induced disturbances of perception, illusions and visual, but sometimes also acoustic hallucinations and synesthesias; profound alterations in time perception; psychomotor inhibition; and variable alterations in affect and thought (Beringer, 1927: 35–97). In his eyes, this symptomatology was sufficiently similar to that of acute schizophrenia to justify the employment of mescaline-induced states as an artificial 'model of psychosis' [*Modell einer Psychose, künstliches Psychosemodell*]. Such a model would allow studying psychoses under controlled experimental conditions on the level of phenomenology as well as objective psychopathology (Beringer, 1927: iv).

Beringer gave Moreau's self-experimentation a pedagogical turn: the majority of the participants in Beringer's trial were medical students and doctors, often Beringer's residents. By serving as test subjects they not only contributed to the methodical production of psychiatric knowledge, but the induction of an artificial psychosis also allowed them to learn about one of the conditions they were meant to treat by way of personal experience.

3 Unlike Beringer, Moreau de Tours had conceived of the hashish intoxication as an artificial delirium, not as a psychosis. The delirium was regarded as the exemplary mental disorder in the first half of the nineteenth century (Healy, 2002: 180; Jay, 1999: 19).

In *Allgemeine Psychopathologie*, Karl Jaspers wrote: 'Since we can never perceive the psychic experiences of others in any direct fashion, as with physical phenomena, we can only make some kind of representation of them' (Jaspers, 1963: 55). In Beringer's model of psychosis, the medium of representation was the self-experimenting subject's own mind. The experience of the mescaline inebriation served as a model of the experience of the acute stages of schizophrenia. This, Beringer hoped, would allow the (future) physicians participating in his trial to share and understand the experience of their schizophrenic patients, which would improve their clinical skills (Beringer, 1927: 31–2).[4]

But, from the 1950s onwards, the similarity of hallucinogen experience and schizophrenia was called into question. In 1957, the British psychiatrist Humphry Osmond noted:

> It is curious that in the lengthy and sometimes heated discussions about the relationship of model psychoses to schizophrenia that smoldered for nearly 50 years, not until 1951 was the difference between a transient, artificially induced, experimental state in a volunteer under laboratory conditions and the prolonged, insidious, creeping illness in an unsuspecting victim whose social life progressively atrophied, clearly recognized. (1957: 421)[5]

According to Osmond, both the hallucinogen experience and the experience of schizophrenia are not only determined by the biological condition but also by the given circumstances. Historically contingent factors such as the subject's assumptions about his or her condition, social relations and the situation in the laboratory shape the experience. The French historian of science Georges Canguilhem has emphasized the artificiality of laboratory conditions as a more general problem of experimental pathology.

> [W]e must not forget that the laboratory itself constitutes *a new environment* in which life certainly establishes norms whose extrapolation does not work without risk when removed from the conditions to which these norms relate. For the animal or for man the laboratory environment is one possible environment among others. Certainly, the scientist is right in seeing in his apparatus only the theories which it materializes, to see in the products used only the reactions they allow; he is right in postulating the universal validity of these theories and these reactions, but for the living being apparatus and products are the objects among which he moves as in an unusual world. It is not possible that the ways of life in the laboratory fail to retain any specificity in their relationship to the place and moment of the experiment. (Canguilhem, 1989: 148–9)

4 Although the training model proposed by Moreau de Tours and Beringer was a subject of discussion throughout the twentieth century and was practiced informally, it has never been developed systematically. Humphry Osmond stated in 1957:

> I know of no study dealing specifically with the application of these substances to the training of the workers engaged in many different disciplines who work together in psychiatry. Such training has resulted from experimental work, but only incidentally. Hyde and others have used these substances to enlarge the sympathy of members of a psychiatric staff for patients in their care. Such a journey of self-discovery may one day be obligatory for those working in psychiatry. Although it might not always be pleasant, with care and understanding this experience would be very useful to the trainee. (Osmond, 1957: 424)

5 Here, Osmond refers to Osmond and Smythies (1952). A systematic argument disputing the comparability of hallucinogen-induced and endogenous psychotic states can also be found in Hollister (1962).

From a historicist point of view, Beringer's experiential model of psychosis can be analyzed as what Michel Foucault called a 'historically singular form of experience' (1997: 199). Foucault proposed to study the historical conditions and, consequently, the limits of possibility of particular experiences by attending to three axes: types of understanding, forms of normativity, and modes of relation to oneself and to others—or knowledge, power and ethics (Foucault, 1997: 199; cf. Jay, 2005: 390–400). Such an analysis allows demarcating the experiences of Beringer's colleagues serving as test subjects from that of his schizophrenic patients. The psychopathologically and pharmacologically literate self-experimenting physicians and medical students had a significantly different understanding of their situation from that of laymen suffering from the unexpected and alienating onset of psychosis. The former were—at least most of the time—well aware of the fact that they had ingested a mind-altering substance and could rely on the limited duration of its effects. To them, the occurrence of psychopathological symptoms was not unsettling and excruciating, but the desirable outcome of a deliberate intervention to be studied with curiosity. A symptom perceived as pathological in a patient appeared as a normal reaction to the given pharmacological stimulus and was interpreted against the background of psychiatric conceptions. The test subjects encountered the medical personnel examining them as colleagues engaged in a common scientific enterprise, not as therapists in a mental institution. And, instead of having to comply with the role of patient, their self-experimentation was part of a heroic professional ethos.

These profound differences called Beringer's experiential model of psychosis into question. Since the 1950s, the influence of the conditions under which hallucinogens were taken or administered on the drug experience has been problematized repeatedly in the discourse on the effects of hallucinogens. Hallucinogens have been described as producing a state of 'heightened suggestibility'. Accordingly, the drug experience is shaped by the experimenter's attitude, the test subject's expectations, as well as the environment in which the experiment takes place. In 1963, Timothy Leary, George Litwin and Ralph Metzner coined the terms 'set' (for mind-set) and 'setting' (for the surroundings) to describe the impact of those factors (Leary *et al.*, 1963). Even though the effects of other drugs, alcohol for example, have been known to depend on the circumstances of consumption as well, no other class of drugs has been regarded as so contingent on set and setting as hallucinogens. A historically and ethnographically oriented epistemology of psychopharmacological research on hallucinogens will have to examine more closely how researchers have dealt with the problems this poses in their experimental practice. The current generation of researchers acknowledges the difference in experience between 'naturally' occurring psychoses and the experimentally induced high. As they are primarily interested in objectifiable neurobiological and neuropsychological aspects of the model psychoses, their claims are significantly less curbed by this difference than Beringer's experiential model. Moreover, they have managed to turn it into an argument *supporting* their hallucinogen model of psychosis. If only set and setting of the drug experience and the onset of psychosis were identical, then, they suggest, the experiences would also be identical:

> [I]f somebody is given psychedelics without his knowledge, then he cannot recognize the artificial nature of his state. When such experiments were performed, the effects were sometimes indistinguishable from acute paranoid-hallucinatory psychoses. The

> situation of a patient with initial acute psychosis is comparable with that of somebody who has ingested psychedelic drugs unknowingly. Both experience pervasive alterations of perception, thinking and affectivity and know nothing about the origin of these alterations. Knowledge of the artificial nature of the state is therefore not a valid criterion for distinguishing between acute endogenous psychoses and psychedelically induced altered states of consciousness. (Gouzoulis-Mayfrank *et al.*, 1998b: 66; see also Hermle *et al.*, 1988: 55)

From the experiential to a descriptive and on to an explanatory model of psychosis

But Beringer's model of psychosis was not merely an experiential model. Based on the first-hand experiences of his test subjects he also established a descriptive model of psychosis. Following Karl Jaspers' psychiatric phenomenology, Beringer attached great importance to the description of the soul 'from inside', drawing from self-observations rather than a psychiatrist's observations of a subject's behavior alone (Jaspers, 1923: 35). The participants of the mescaline trial were supposed to produce written reports of their experiences. By collecting and analyzing these reports (which have been published in the appendix of *Der Meskalinrausch*, 1927) Beringer produced an ideal-typical phenomenological account of the psychosis-like effects of mescaline. Following Rachel Ankeny's article 'Fashioning descriptive models in biology' (2000), such a description can itself be regarded as a pre-explanatory or descriptive model of mescaline inebriation, which, in turn, served as a model of psychosis. Hence, the descriptive model can be said to function as a second-order model of psychosis. In order to fulfill this function, the description had to emphasize those properties that the intoxication had in common with psychotic, particularly schizophrenic, episodes.

As a descriptive model Beringer's phenomenological account was arrived at by means of abstraction. What was presented as the prototype of mescaline inebriation is, in fact, an ideal-typical construct. It presents a certain pattern of recurring symptoms, which Beringer brought out by analyzing the reports from approximately 60 experiments. From these he tried to extrapolate what mescaline did as such—independent of the individual subjects and situations. The multitude of responses the drug provoked in different individuals at different points in time made it particularly difficult to identify the properties that were to be attributed to the drug itself. However, Beringer claimed that, by looking at a sufficiently large number of experiments, he had been able to extract a recurrent set of symptoms, which he identified as effects of the drug (as opposed to those produced by the states and traits of the test subjects) (Beringer, 1927: iii). Andreas-Holger Maehle describes a very similar approach for self-experiments with opium in the eighteenth century, in which a form of scientific objectivity was achieved by way of collectivization of subjective experiences:

> Overall, the example of opium research shows how different, at first contradictory observations in self-experiments contribute to the development of a kind of collective subjective experience eventually condensed to a profile of action of the drug. Thereby, subjectivity is elevated to a new form of scientific objectivity. (Maehle, 1995: 294)

The object of this objectivity was subjective self-observations. But Beringer anticipated that eventually his description of the analogies between mescaline inebriation and acute stages of schizophrenia would serve as a basis for an investigation of the physical foundations of the psychopathological phenomena that these conditions have in common. He hoped that, one day, biochemical research on the effects of mescaline might 'reveal to us the disorders of intermediary metabolic processes (autointoxication process, endocrine metabolic toxins, etc.) in the acute phase' of schizophrenia (Beringer, 1927: 114). But his own approach did not provide the means to directly examine the biological substratum of the psychoactive effects of mescaline. The life processes underlying the effects of mescaline and the existence of hypothetical endogenous psychotogens remained purely speculative. As a phenomenological psychiatrist following Jaspers, Beringer was neither eager to push this kind of theorizing much further, nor did he make an effort to study the biochemistry of mescaline intoxication and schizophrenia himself. But other researchers used his account as a framework for the exploration of explanatory questions (cf. Ankeny, 2000: 267). The shift from Beringer's descriptive, pre-explanatory model to explanatory models of psychosis took place in the 1950s. At the time, several groundbreaking discoveries and innovations in the field of psychopharmacology initiated a process of reorientation of psychiatry toward the life sciences.

Especially important were the discoveries of the antipsychotic chlorpromazine by the French company Rhône-Poulenc in 1951 and of lysergic acid diethylamide (LSD) by the Swiss pharmaceutical company Sandoz in 1943. LSD temporarily became one of the most important research tools in psychiatry. Against the background of Beringer's work on mescaline, its hallucinogenic effects were also interpreted as a model of psychosis. But, unlike mescaline, LSD turned out to be effective in extraordinarily low doses. Therefore, it did not make sense to assume that it affected all cells in the brain and in the rest of the body alike. Instead, a specific target mechanism was postulated, which eventually led to the concept of specific receptors on the surface of neurons that interact with molecules such as LSD as well as endogenous substances. Chlorpromazine not only helped to alleviate some of the symptoms of schizophrenia, it was also capable of inhibiting the effects of LSD. With these two substances an experimental system seemed to emerge that would allow exploring causes as well as potential treatments of psychosis in healthy volunteers in controlled settings. Psychiatry, it was hoped, would finally get the chance to meet some of the scientific standards already governing other medical subdisciplines and the life sciences (Healy, 2002). The 'molecularization of psychiatry' had begun (Rose, 2003: 5).[6]

This constituted the contemporary form of what Nikolas Rose—following Ian Hacking and Ludwik Fleck—has called 'the ''style of thought'' of biological psychiatry' (2003: 3). This new way of thinking entailed a reconceptualization of the causes, and consequently the therapies, of mental illness. Instead of focusing on the patients' subjectivity—their dreams, memories, associations, etc. in psychoanalysis, and their abnormal ways of experiencing the world in phenomenological psychiatry—their suffering was now attributed to a neurochemical disorder of the brain, to psychopharmacologically correctable molecular errors.

6 Page numbers for Rose (2003) refer to the pdf available on the Internet.

> In this process, psychiatry claims to have overcome, at last, the Cartesian dualism of body and soul. The deep psychological space that opened in the twentieth century has flattened out. In its new 'neurochemical' account of personhood, psychiatry no longer distinguishes between organic and functional disorders, with only the former being thought of as somatic. It no longer concerns itself with the mind or the psyche. Mind is simply what the body, what the brain, does. (Rose, 2003: 10)

In 1949, the Swiss psychiatrists Roland Fischer and F. Georgi took up the analogy of hallucinogen intoxication and schizophrenia described by Beringer while introducing a differentiation. Mescaline, they claimed, produced a state resembling the catatonic form of schizophrenia, while LSD provoked a hebephrenic variant. From this they inferred a toxic genesis of schizophrenia. An error in the metabolism of the liver, they postulated, produced an 'endogenous autotoxin' triggering schizophrenic episodes. Beringer's descriptive model of psychosis led them to propose an explanatory model based on the hypothesis that different forms of schizophrenia were caused by different toxic metabolites (Fischer *et al.*, 1951; Vannini and Venturini, 1999: 191).

While Beringer had only speculated about this, Fischer and Georgi tested their assumption experimentally by examining metabolic disorders provoked by mescaline and LSD, especially the effects of these drugs on liver functions. In a similar vein, a number of researchers, especially in the United States and Canada, hypothesized various metabolites as potential agents in the pathogenesis of schizophrenia. The most elaborate and prominent postulate was the transmethylation hypothesis by Abram Hoffer, John Smythies and Humphry Osmond who suspected an erroneously methylated hallucinogenic derivate of adrenaline to be the cause of schizophrenia (especially for Canada, see Dyck, 2005; Healy, 2002: 182–91; Hoffer and Osmond, 1959; Hoffer *et al.*, 1954). The emergence and consolidation of this explanatory model of psychosis entailed not only the production of hypotheses, but also of experiments to verify them. It thereby triggered a significant amount of scientific activity, which aimed at finding psychotogenic metabolites resembling mescaline and LSD.

Being based on the assumption of congruence of phenomenology and mechanism, this step from a descriptive to an explanatory model was daring. Canguilhem refers to a debate over sleeping pills, in which A. Schwartz argued that '[i]t would be wrong to believe that sleep brought by pharmacological means and normal sleep necessarily have an *exactly similar phenomenology*' adding that '[i]t must be admitted that artificially inducing sleep by interfering with the nerve centers does not enlighten us as to the mechanism by which the hypnotic center is naturally put into operation by the normal factors of sleep' (Canguilhem, 1989: 148). What is being problematized here is the relationship between phenomenological description and biological explanation. An analogous problematization has occurred in the context of model psychoses. LSD and mescaline, it turned out, pharmacokinetically induce tolerance. If an LSD-like substance was indeed responsible for schizophrenia, the disease should subside within a few days—which it does not (Vannini and Venturini, 1999: 207). However, as Healy indicates, the quest for metabolites involved in hallucinogen intoxications as well as schizophrenia might also have been given up for lack of economic incentive: unlike the dopamine hypothesis of schizophrenia, which will be discussed below, the transmethylation hypothesis did not help to market

any drugs (Healy, 2002: 192). For whatever reason, the first explanatory model derived from the descriptive model of psychosis did not produce the expected results and was abandoned.

The preliminary end of model psychosis research

Throughout the 1950s, hallucinogens attracted much scientific attention. By 1961, more than 1,000 articles had been published in medical journals on LSD alone (Dyck, 2005: 383). The newly developed antipsychotics significantly reduced the rate of institutionalization among schizophrenic patients and enabled them to live in their communities receiving outpatient treatment. However, most of them suffered from distressing and stigmatizing side effects (Estroff, 1981; Healy, 2002: 233, 343 f.). Model psychosis research promised to find the causes of schizophrenia and to develop more specific medications sparing patients the severe side effects of the first generation of antipsychotic drugs. Notwithstanding, only a decade later, model psychosis research had virtually come to an end. There were two reasons for this surprising twist: a tightening up of regulations and an impasse in the research agenda.

On the one hand, the use of hallucinogens had been subjected to much stricter regulations. In part, these restrictions were the result of a general tightening of controls of pharmaceuticals mostly triggered by the thalidomide scandal in 1960–61. But the constraints on hallucinogens had become considerably more severe since they had gained popularity among college students and members of the counterculture. A series of sensationalist newspaper articles was published, in which the consumption of hallucinogens was associated with psychotic reactions, suicide and murder. This eventually led to their being made illegal at the end of the 1960s (Braden, 1970; Davenport-Hines, 2002: 332–3; Jonnes, 1996: 259; Stevenson, 1987: 274) However, not only private hallucinogen consumption, but also academic hallucinogen research began to be regarded with suspicion when certain scientists, like the Harvard psychologist Timothy Leary, began to advocate the widespread use of hallucinogens beyond the walls of the laboratory. Even though model psychosis research as such did not endorse the consumption of hallucinogens—after all, it presented them as substances that caused hardly desirable states of psychosis—it became more difficult to gain approval for the application of hallucinogens in clinical trials, no matter what the underlying assumptions were. Researchers were discouraged by more and more bureaucratic hurdles. The more precarious their area of research was considered, the more carefully they had to design their research protocols and the more audit and record-keeping they were expected to do. Such conditions created a situation in which the individual scientist was still free to choose what he or she wanted to work on, but at the same time these choices were guided in subtle (and not so subtle) ways. Furthermore, the manufacture of hallucinogens had begun to impair the image of Sandoz, which had provided the required drugs to researchers. Soon Sandoz shut down its production. The pharmacologist Oakley Ray remembered in an interview:

> I was also running LSD, psilocybin and mescaline studies in rats but then Sandoz decided to get out of that business. Back then, if you wanted LSD for your research, you picked up the phone and called Rudi Bircher at Sandoz and said, 'Rudi, I need

> 100 ampoules of LSD.' He'd send you them or whatever else you wanted if Sandoz produced it. When they got out of that business, you could still get what you needed from the government but it meant a lot of paperwork and it wasn't worth it. So I scratched that whole line of research. (Healy, 1998: 438)

Ray's explanation for having given up hallucinogen research raises the question why he felt that the paperwork was not worth it. Only a decade earlier, it had been perceived as one of the most promising directions of psychiatric research. First, all attempts to substantiate evidence that one of the supposedly schizophrenogenic metabolites was actually playing a significant role in the pathogenesis of schizophrenia had failed. In the meantime, the metabolic model had been replaced by another explanatory model—that of neurotransmission as a chemical process between nerve cells. As Rose put it:

> Initially, it had been thought that although nerves themselves transmitted signals by chemical means, transmission across the synapse was electrical. By the 1960s, largely as a result of work on the new psychiatric drugs—first the antipsychotics such as chlorpromazine, then the antidepressants such as imipramine and iproniazid—not forgetting the experiments with lysergic acid diethylamide—it had been accepted that neurotransmission was carried out by chemicals [such as dopamine, serotonin, or glutamate]. (Rose, 2003: 11)

Hence, the molecular errors to which mental disorders like schizophrenia were attributed changed in nature. Now a lack or a surplus of certain neurotransmitters or their receptors, and a resulting overstimulation or decreased activity of certain neurotransmitter systems, were held responsible. The concept of neurotransmission brought together the realm of (pathological) life processes and that of (erroneous) information-processing. Disorders of perception, cognition and affect, which schizophrenia and hallucinogen-induced states have in common, could now be explained as errors in neural information-processing.[7] As the German psychiatrists Leo Hermle *et al.* would write two decades later:

> A neurobiochemical disorder might also explain the known impairment of information processing, of selective filtering, and decoding of experiences from long-term memory, which can be grasped psychopathologically as so-called basic syndrome [*Basisstörungen*]. A similar biochemical and neuropsychological functional disorder might underlie the so-called model psychoses. (Hermle *et al.*, 1988: 53)

The explanatory model of schizophrenia changed accordingly. The idea that schizophrenia was caused by a toxic metabolite was replaced by the so-called dopamine hypothesis. In the 1960s, the work of Arvid Carlsson, Margit Lindqvist, Jac van Rossum and others had suggested that schizophrenia was the direct consequence of an overactivity of dopaminergic neurons in the brain. But only in the 1970s, when the first receptors had been isolated and

7 In terms of information theory, psychotic states were now characterized by 'a gross flaw in the filtering, matching, and correlating of sensory inflow, which some believe to be the primary defect. If the accurate computation of sensory information broke down, or if the normal overload of incoming data failed to be eliminated, a schizophrenic state could result' (Cohen 1972: 88). At the intersection of molecular biology and information theory, the concept of error became a central element of our understanding of life. In the second half of the twentieth century, Canguilhem argues, there is 'no difference between the error of life and the error of thought, between the errors of informing and informed information' (1989: 277). Interconnections between the concept of information in molecular biology and the exploration of the mind with the help of hallucinogenic drugs are discussed by Doyle (2002).

the pharmaceutical industry began to advertise its antipsychotic drugs by pointing out that all known antipsychotics bound to dopamine receptors, did the dopamine hypothesis of schizophrenia gain more widespread support (Healy, 2002: 207–19). Neither the classical hallucinogens like mescaline and LSD, nor psilocybin, nor a newly discovered group of substances comprising phencyclidine (PCP) and its congener ketamine (which, on the phenomenological level, was said to model schizophrenia even better) fit into this scheme. The hallucinogenic effects of mescaline, LSD and psilocybin (or rather its psychoactive derivate psilocin) were found to be primarily mediated by a particular subtype of serotonin receptors (5-HT_{2A}), while PCP and ketamine were shown to possess an anti-glutamatergic activity at NMDA receptors.[8] None of them demonstrated a predominant dopaminergic activity. Hence, when the dopamine hypothesis of schizophrenia became paramount in the 1970s, the use of hallucinogen-induced states as models of schizophrenic psychoses stopped making sense. The model psychosis researchers affected by the severe regulatory constraints on hallucinogen research did not have enough confidence in their research agenda anymore to resist the political and regulatory pressure on their work.[9] The human experimentation with hallucinogens died down in scientific institutions. Those who had always doubted the analogy between hallucinogen inebriation and psychosis took this development as an affirmation of their criticism. The use of hallucinogens as a means of modeling psychoses appeared to be an impasse.

The present: revival of model psychosis research

During the 1980s, the dopamine hypothesis of schizophrenia was relativized by more and more psychiatric researchers when it became clear that schizophrenia could not be explained by hyperactivity of the dopaminergic system alone.[10] Eventually, it was supplemented by two other postulates: the serotonin and the glutamate hypotheses. There was evidence that, apart from the dopamine system, these neurotransmitter systems were also involved in the pathogenesis of schizophrenia. All of a sudden, hallucinogen-based models of psychoses seemed to make sense again. As the dopamine hypothesis had not been refuted altogether, the claims had to be articulated in a more modest fashion now. On the one hand, 5-HT_{2A} agonists like psilocybin could be used to model certain aspects of schizophrenia related to the putative underlying disorder of the serotonergic system (especially so-called positive symptoms such as hallucinations and disorganized thought, speech and behavior). The effects of anti-glutamatergic hallucinogens like ketamine, on the other hand, could serve as models of supposedly glutamate-related deficits in schizophrenia

8 Dopaminergic pathways could be activated by stimulants such as amphetamines and cocaine, which were also known for their (unreliable) potential to provoke psychoses when administered repeatedly and in high doses. In fact, their psychotogenic potential served as one of the main arguments in favor of the dopamine hypothesis. However, because of the harmful effects the required doses had on test subjects and because of the unpredictable outcomes of such experiments, amphetamine intoxications did not gain currency as a model of psychosis in experimental psychiatry (cf. Healy, 2002: 119 and Gouzoulis-Mayfrank, personal communication).

9 This narrative is based on Gouzoulis-Mayfrank (personal communication).

10 Especially, research on the effects of atypical antipsychotics such as clozapine produced evidence that the dopaminergic system could not be the only neurotransmitter system involved in the pathogenesis of schizophrenia (Healy, 2002: 219–24).

(also comprising negative symptoms like emotional blunting, apathy and attention abnormalities) (Gouzoulis-Mayfrank *et al.*, 2006).

After two decades, the political climate had changed as well. As time passed by, the clash of worldviews that had dominated the controversy over hallucinogens in the 1960s and 1970s lost momentum. When a German group of psychiatric researchers around Leo Hermle, Manfred Spitzer and Euphrosyne Gouzoulis-Mayfrank picked up model psychosis research at the end of the 1980s, they did not encounter much resistance. In fact, they had been encouraged by Rudolf Degkwitz, the director of the psychiatric clinic of the University of Freiburg, and received funding from the Deutsche Forschungsgemeinschaft [German Research Foundation] (Gouzoulis-Mayfrank, personal communication).[11] From the very beginning, the revival of hallucinogen research in German biological psychiatry took place in a framework of well-established institutions rich in symbolic as well as financial capital.[12]

From 1988 onward, the group around Hermle, Spitzer and Gouzoulis-Mayfrank published a series of historically oriented review papers on model psychosis research (Hermle *et al.*, 1988, 1992b, 1993). Between 1988 and 1989, they also ran a pilot study, in which they administered mescaline (still from Beringer's stock) to twelve healthy volunteers to explore the psychopathology induced by mescaline. These papers served two purposes: first, they mapped the territory providing orientation to the authors as well their scientific community. Second, in order to ensure support for their project of reviving model psychosis research among their peers, it was particularly important to refute the criticism by Osmond, Hollister and others that had called into question whether the symptoms of hallucinogen intoxications and schizophrenia were sufficiently similar. The Hermle group pointed out that visual hallucinations were not uncommon among schizophrenics, while acoustic hallucinations could also be provoked by hallucinogens. They also had to respond to the objection that schizophrenics who had already taken hallucinogens reported that their drug experiences had been altogether different from their psychotic experiences. With her article on psychedelic experiences in the early stages of schizophrenic episodes, Gouzoulis-Mayfrank went to the heart of the matter of the conflict of worldviews that had been sparked off by the hallucinogens. By demonstrating that the ecstatic and transcendental experiences reported by many users of hallucinogens could also occur in the early stages of schizophrenia, Gouzoulis-Mayfrank asserted the phenomenological similitude of early and acute stages of psychosis and hallucinogen effects (Gouzoulis-Mayfrank *et al.*, 1994). The Hermle group considered the use of hallucinogen-induced states as models of psychosis as particularly useful because it provided the possibility of intraindividual

11 When Gouzoulis-Mayfrank introduced model psychosis research to the university clinic in Aachen in the early 1990s, she initially had to face critical questions by the ethics committee—a control mechanism that had only come into existence in the 1960s, at about the time when model psychosis research was already about to come to an end (Rothman, 1991). In a personal communication, Gouzoulis-Mayfrank underlined that the difficulties she encountered initially in her discussions with the ethics committee in Aachen were not politically motivated.

12 In the United States, the situation was different. I will address the conditions under which hallucinogen research was relaunched in America elsewhere.

comparisons and eliminated the impact of prolonged courses of mental illness on the symptomatology (e.g. the development of coping mechanisms) (Hermle *et al.*, 1992a: 976f.). The hallucinogen inebriation, they hoped, would allow them to observe nascent psychoses.

But the Hermle group did not content itself with psychopathological descriptions. By applying the new tools of contemporary cognitive neuroscience to the old concept of model psychosis they also hoped to advance the understanding of the biology of schizophrenia. In 1988, Hermle *et al.* concluded:

> The remarks above have shown that so-called model psychoses indeed resemble so-called 'endogenous' schizophrenias on the level of psychopathology. They are also comparable with respect to genesis although caveats apply. Principal differences asserted in the past cannot be maintained or need to be called into question. Therefore, it is desirable that experimental psychosis research is continued with the methods of neurophysiology, biochemistry, and psychopathology available to us today. For this reason, neuropsychology will become particularly important, with its dynamic tachistoscopic techniques and correlated neuroradiological (PET, SPECT) and neurophysiological (EEG techniques, BEAM) methods: Neuropsychology can detect psychotic alterations 'prephenomenally' between biochemistry on the one hand and psychopathology on the other hand closest to the substrate. (Hermle *et al.*, 1988: 56)

Filtering deficits, animal models and a reconfiguration of anthropos

Neuro- and pharmacopsychology as practiced in contemporary model psychosis research emerged from the tradition of Wilhelm Wundt's experimental psychology. Before Wundt, psychology for the most part had been based on introspection. Wundt, in contrast, argued against self-observation as a means of studying the mind and proposed to use the methods of physiology to find answers to well-defined questions under carefully specified conditions (Wundt, 1904: 1–38). Wundt's student, the psychiatrist Emil Kraepelin, employed his teacher's experimental techniques to study the effects of drugs on psychological functioning. In his 1892 study *Ueber die Beeinflussung einfacher psychischer Vorgänge durch einige Arzneimittel*, he described the psychophysiological or 'pharmacopsychological' effects of alcohol, tea, morphine, ether and other drugs on 'simple psychic processes' in test subjects (Kraepelin 1892; Pieper, 1999: 80). What is characteristic of Kraepelinian experimental pharmacopsychology is that it takes simple, easily operationalizable and quantifiable mental functions as its objects, measuring reactions to systematic presentations of well-defined external stimuli under the influence of drugs. Contemporary neuropsychopharmacology has remained true to these principles. By returning to Kraepelin's experimental approach, today's psychopharmacologists have replaced or supplemented the meticulous psychopathological description of experience that had been the focus of Beringer's model of psychosis with the measurement of clear-cut neuropsychological and neurobiological parameters. Experimental pharmacopsychology produces quantitative results, which allow for further statistical processing and which are supposed to be independent of the test subjects' subjectivity and the observer's vocabulary. This refashioning of the technologies of psychiatric

truth has established a form of psychiatric research which meets the standards of biomedical knowledge production, helping psychiatry to overcome its image as a pseudoscience and to obtain research funds.

The 'simple psychic processes' that have been the focus of attention in the latest episode of model psychosis research are different aspects of 'sensorimotor gating'. The term 'sensorimotor gating' refers to filtering mechanisms in the processing of sensory information by the central nervous system, which are meant to protect the organism from being overwhelmed by the amount of information constantly being registered by its sense organs. The most widely studied measure of sensorimotor gating is prepulse inhibition (PPI). The concept of PPI describes the following phenomenon: sudden and intense sensory stimuli trigger a startle reflex, which comprises nictation as well as a jerk of the whole body. If a weak, non-startling stimulus (e.g. a low noise referred to as prepulse) precedes the stimulus (e.g. a loud noise referred to as pulse), it inhibits the startle response. The amplitude of the electromyographically registered blink reflex is reduced. This is called prepulse inhibition or PPI (Graham, 1975: 238–48). PPI serves as an operational measure for sensorimotor gating. In *Dementia praecox oder die Gruppe der Schizophrenien* (1911), Eugen Bleuler described an impairment of attention in schizophrenic patients, postulating that this might lead to a reduced ability to filter out irrelevant stimuli. In the 1970s, David Braff, Mark Geyer and others began to employ PPI to examine the attentional and information-processing dysfunctions of schizophrenics psychometrically. They interpreted the reduction of PPI in schizophrenic patients as the prephenomenal correlate of the phenomenologically described impairment of attention reported by Bleuler. A breakdown of the hypothetical perceptual filter, and the subsequent overload of information and sensory stimuli, has been presented as an explanation for a number of symptoms of schizophrenia such as distractibility, misperceptions and formal thought disorders (Meincke *et al.*, 2001: 844–52).

Certain 'simple psychic processes'—PPI among them—turned out to be based on aspects of neural information-processing elementary enough to be shared by all mammals. Since psychiatry has begun to concentrate on the brain instead of the human mind as its primary scientific object, it has become reasonable to use animal brains as models of human brains, presupposing that human neurobiology does not differ fundamentally from that of other mammals. If a reduced PPI is regarded as a neural correlate of schizophrenia, a rat displaying a reduced PPI can be taken as an animal model of this mental illness. From the mid 1970s onwards, Geyer and others studied the startle response in rats that had been administered hallucinogens. They found that it augmented the startle response and impaired its habituation. Based on this finding, rats on hallucinogens are now used as an animal model of psychosis.

Transplanting the biologized concept of model psychosis into the realm of animal experimentation has been presented as particularly promising because hallucinogen-based animal models of schizophrenia might facilitate the discovery and development of new antipsychotic drugs. For ethical reasons, new pharmacological agents need to undergo extensive testing before they can be applied to humans even in preclinical experimental settings. The research and development process is too expensive and time-consuming if there is no indication that a new drug might work. But how can one tell if it is not permissible to test a new drug in humans? A drug's potential to reverse hallucinogen-induced filtering deficits and

similar parameters in animal models enables researchers to screen new drugs and to identify those that might have antipsychotic effects. As the Swiss psychiatrist and psychopharmacologist Franz Vollenweider has pointed out, these hopes and promises to find novel treatments to alleviate the suffering of schizophrenics have contributed significantly to the recent revival of hallucinogen research:

> [T]he similarity of PPI deficits in animal studies and schizophrenic patients, in combination with other findings, has revitalized interest in hallucinogens in the 1990s and prompted a concerted search into the neurotransmitter systems involved in modulating PPI in rodents. (Vollenweider, 1998: 29)

This new perspective leads to a radically different conception of mental illness. The tragic perspective on madness, from which madness was seen as revealing a deeper truth about the human condition (Foucault, 1965), Freud's explanation of Schreber's psychosis as a defense against homosexual love for his father or the phenomenological attempts to *understand* a psychotic's mental life have given way to a conception of schizophrenia as a disorder of the brain based on an error in neural information-processing. Human beings are animals through and through—even in the realm of thought. They share the neurobiological basis of their cognitive processes with other mammals. This change in psychiatric style of thought goes along with a reconfiguration of the figure of *anthropos*. The blurring of the boundary between the human and the animal on the level of neurobiology makes it seem reasonable to employ animal models to explore the foundations of mental illness.

Nonetheless, by transplanting the hallucinogen model of psychosis into the animal kingdom (creating a second-order model of psychosis, i.e. an animal model of the hallucinogen model of psychosis) its epistemological limitations became even more apparent. For example, in 1982, Jon Koerner and James Appel demonstrated that, in drug discrimination tasks, rats fail to recognize 'hallucinogenicity' as a property shared by psilocybin, LSD and mescaline. They concluded that animals might experience the effects of hallucinogens in a very different way than humans (Koerner and Appel, 1982). Additionally, further research on PPI has qualified the applicability of findings in laboratory animals to human patients. When measuring the PPI of healthy human subjects on psilocybin Gouzoulis-Mayfrank *et al.* found—against their expectations—that, unlike schizophrenics and rats on psilocybin, their test subjects showed an *increased* PPI (Gouzoulis-Mayfrank *et al.*, 1998a).[13] In this puzzling case, the animal model of psychosis adequately represented its object, i.e. schizophrenia, whereas its human counterpart failed to do so. It remains to be seen how model psychosis researchers are going to respond to this conundrum. In the meanwhile, we need to content ourselves with a remark by Mark Geyer in his article 'Why study hallucinogenic drugs in animals?':

> It is not necessary to argue that hallucinogens mimic all the symptoms of a complex disorder such as schizophrenia to believe that they affect some of the brain systems that can be disturbed in psychiatric illnesses. Thus, an understanding of hallucinogen actions may be relevant to specific aspects of schizophrenia rather than the entire complex syndrome. (1998: 33)

13 Vollenweider *et al.* (1999) have reported similar results for MDMA.

Conclusion: 'Ceci n'est pas une psychose'

On his famous 1928–9 painting of a pipe, entitled *La Trahison des images*, the French surrealist René Magritte wrote: '*Ceci n'est pas une pipe*'—*This is not a pipe*. The apparent discordance between the image and the statement can be solved easily. After all, what can be seen is an image of a pipe and not a pipe.[14] Similarly, one might say about the hallucinogen model of psychosis: '*Ceci n'est pas une psychose*.'

Beringer had been cautious not to overextend his assertion that there was a phenomenological resemblance between mescaline intoxication and schizophrenia. But he did not want to claim an identity between the intoxication psychosis [*Intoxikationspsychose*] induced by the drug and schizophrenia proper unless the biochemical substrates of the two states had been identified. From the 1950s onward, the experiential identity of schizophrenia and the hallucinogen high was repeatedly called into question. After almost a century of model psychosis research, there seems to be a consensus today that, from a neurobiological point of view, hallucinogen intoxications and schizophrenia are distinct phenomena. No matter what the indexical refers to—the hallucinogen experience or the underlying biology—one might conclude that 'this' is not a psychosis—at least not a schizophrenic one.[15]

However, hallucinogen intoxication does not have to be identical to the mental disease to serve as a model of schizophrenia. In fact, the definition of a model requires that it *cannot* be identical with its object. Hence, from a purely epistemological point of view, the distinctness of hallucinogen inebriation and schizophrenia does not refute the conception of the hallucinogen model of psychosis. In his book *Models*, Wartofsky writes:

> The business about degrees of approximation is also a shabby complaint, if one keeps in mind a simple constraint on models, which we take as a definition (or part of one), or as a convention: nothing which is a model is to be taken as a model of itself, nor of something identical with it. (1979: 4)

Wartofsky reminds his readers that they need to 'keep in mind the metaphorical nature of [...] models, and remember to distinguish the model from what it is a model of'. Emphasizing the 'metaphorical nature' of models raises the question: 'Are models ever

14 For a more intricate discussion of the relationship of representation in Magritte's painting, see Foucault (1998) and Morstein (1983).

15 For the sake of greater conceptual precision, this article would have to be entitled less elegantly '*Ceci n'est pas une schizophrénie*'. As Franz Vollenweider pointed out in a discussion: 'There is no doubt that hallucinogens cause a psychosis. This is the case *by definition*. There is nothing to be compared [between inebriation and psychosis because they are identical]. [...] In psychiatry all forms of ego-dissolution (including religious experiences) are pathological' (Vollenweider, personal communication, my translation—NL) Vollenweider interprets the model character of the hallucinogen model of psychosis within the conceptual framework of modern psychiatry as one kind of psychosis (drug-induced) serving as the model of another kind of psychosis (schizophrenia). However, the identification of the state induced by hallucinogens with psychosis can be subjected to a nominalistic critique. Only after the introduction of the concept of psychosis by Karl Friedrich Canstatt and Ernst von Feuchtersleben in the 1840s could certain odd states of mind be defined as 'psychotic'. In 1908, Karl Bonhoeffer argued that a broad range of 'exogenous', i.e. extracerebral, factors, including poisons, could produce the clinically largely uniform syndrome of symptomatic psychosis. On this basis, it has become conceivable to define drug effects as a form of 'psychosis'. From this angle, *Ceci n'est pas une psychose* can also refer to the dissimilarity between name and corresponding reality.

"true", i.e. is a model ever a true representation of its object?' (1979: xx). Wartofsky answers this question by elaborating his concept of representation:

1. *Anything* (in the strongest and most unqualified sense of 'anything') can be a representation of anything else. Therefore, there are no intrinsic or relational properties which mark one thing off as a representation of something else; or [...] everything has infinitely many properties in common with everything else, and so anything can be taken as a representation of anything else in terms of some of these shared properties.
2. It is *we* who constitute something as a representation of something else. It is essential to something's being a representation, therefore, that it be *taken* to be one.
3. From (1) and (2) it follows that a representation is whatever is taken to be a representation; that representing is something *we do*, and that nothing *is* a representation except insofar as we construct or construe it as one; and in this, it is precisely the representation we make it, or take it to be. (1979: xx f.)

But Wartofsky also argues that

> ... the essential feature of the modelling relationship [...] is that, although it is the case that anything may be taken as a model of anything else, it is *being taken as a model* which makes an actual out of a potential model; and every case of *being taken as a model* involves a restriction with respect to *relevant properties*. Not everything has the relevant properties which permit it to be taken as a model of something else, if relevance has to do with our *purposes* in taking something as a model. (1979: 6)

Thereby, Wartofsky shifts the argument from a discussion of 'what representations *are* to the consideration of the human activity of *representing*' (Wartofsky, 1979: xxi; see also Giere, 2004). Modeling entails that the person making and using the model interprets the relationship between the model and its object in a certain way. Unlike all the other things that have properties in common with the object, the model is considered to be a good model because it shares a *particular* set of features with the object. The choice of these features—and, hence, of the model itself—is a normative act presupposing a certain practical orientation or aim.

Considering that models of psychosis serve a certain purpose, the relationship between these models and their object is regarded as contingent, but not arbitrary. Sidney Cohen, an American physician who had been involved in model psychosis research in the 1950s wrote:

> The debate about whether LSD brings forth a model psychosis is rather futile; undeniably, it can induce a model of psychosis, but for the reasons mentioned it cannot duplicate schizophrenia. A model need not reproduce every aspect of the thing modeled. For example, a model of a bridge, in addition to its difference in size, is also of different material and construction. Nevertheless, it is possible to learn much about the actual bridge from it. Just so, much can be learned about schizophrenic symptoms from a study of LSD phenomena. (Cohen, 1972: 92–3)

In the 1990s, Spitzer articulated a genuinely pragmatist concept of model with respect to neural networks as models of the brain:

> If models did not simplify matters, they would not be models but, instead, reality itself. Models have a right to exist insofar as they are simple.
>
> A good model represents only those aspects of a complex data set that are essential from a certain perspective. [...] Models are therefore neither true nor false. Instead, they are useful or not. (Spitzer, 1999: 295–6)

The project Gouzoulis-Mayfrank has been pursuing persistently—by now, her colleagues Hermle and Spitzer have changed course—is a comparison of the effects of different hallucinogens to evaluate and differentiate their usefulness for the purpose of modeling different kinds and aspects of psychoses.

> The pharmacological models, which we have, are models of different quality for different syndromes. The two main models are the serotonergic and the anti-glutamatergic model, which model different psychotic syndromes. Therefore, it is reasonable to examine and compare the different models. Supposedly, the neurobiological mechanisms of psychoses play different roles in the different models as well as syndromes. By examining a serotonergic as well as an anti-glutamatergic—and, if you like, also a dopaminergic—model we can test whether certain neurobiological parameters can be found in different models of psychosis or only in a single one. This produces clues concerning the connections between neurobiological parameters and types of psychosis. [...] For this reason, it is very reasonable to use different models. One can say: 'With this substance we model this syndrome and with that substance another one.' (Gouzoulis-Mayfrank, personal communication)

Even though Gouzoulis-Mayfrank is convinced that the 'model psychosis paradigm is potentially valuable as a way of validating basic neurobiological concepts thought to be related to schizophrenia' (Gouzoulis-Mayfrank *et al.*, 1998b: 67), she does not assume that schizophrenia and its drug models were based on an identical neurobiological substrate. The commonalities between the two are not presupposed, but investigated. Moreover, what is found in the hallucinogen models is not believed to prove anything about the nature of psychoses, but can only serve as a hint inspiring further research in schizophrenic patients. In Gouzoulis-Mayfrank's eyes, the purpose of these models is the following:

> They are meant to give interesting clues, which then need to be verified in patient populations. However, the models only serve as supplements. Based on model psychoses alone nothing can be demonstrated. There is no way of safely extrapolating from the results of model psychosis research to mechanisms of psychosis. Hence, I need to check whether a model fits and if it does, then I have only gained another argument. (Gouzoulis-Mayfrank, personal communication)

What is peculiar about these models as models is that they do not function as transparent representations of their object. Although object and model are distinct, they are situated on the same ontological level. In Beringer's experiential model of psychosis, it is an

experience that serves as the model of another experience, while its neurobiological remake presents a brain on hallucinogens as the model of a psychotic brain. In comparison to other kinds of models, this seems remarkable. Mathematical models of economic development, wiring diagrams of the nervous system of *C. elegans* (which Ankeny presents as an example of descriptive models), or three-dimensional models of molecules are qualitatively different from their objects in the 'real world'. The latter are formal, not material models. They are independent of their physical embodiments. The representations are not made of the same stuff as what they represent. In the case of the model psychoses, on the other hand, this ontological difference has been eradicated. Possessing a distinct materiality and depth, model psychoses function as scientific objects in their own right. They have a certain opacity calling for research on the model itself (while it is not necessary to chemically investigate the materials from which the model of a molecule has been built). This opacity allows for surprises, like the increased PPI in human subjects on hallucinogens, and, at times, it thwarts the purposes that the scientists had in mind for their model.

As a scientist taking something as a model of something else has a particular end in view, Wartofsky argues—a model is oriented toward a certain achievement in the future. Therefore, he claims, a model is a 'technology for creating the future'. By the phrase 'creating the future' he means '*acting* in such a way as to make the future conform to some present vision of it' (Wartofsky, 1979: 142 f.). However, the hallucinogen intoxications are phenomena that have turned out to be too complex to meet all expectations of those using them for the purpose of modeling psychoses. The model psychosis can be looked at as what Hans-Jörg Rheinberger has called an experimental system. Experimental systems are 'the basic, functional units of scientific activity' (Rheinberger, 1999: 418). An experimental system needs to be stable enough to maintain and reproduce itself, while being flexible or loose enough to promote unpredictable events. As a research system, it can only keep going if it generates not only knowledge but also 'the unknown', which requires further research to be explained.[16] Following the molecular biologist François Jacob, Rheinberger has characterized such set-ups as 'machines for making the future'. They are not simply experimental devices that generate answers: experimental systems are first and foremost vehicles for materializing questions' (Rheinberger, 1997: 28). Thus, Rheinberger's characterization of experimental systems is highly reminiscent of Wartofsky's branding of models as 'technologies for creating the future'. But, unlike Wartofksy, Rheinberger has an open future in mind, a future that cannot be foreseen and that, almost by definition, will not 'conform to some present vision of it'. As Gouzoulis-Mayfrank has pointed out, hallucinogens cannot answer any questions about psychoses. As a model of psychosis they can only produce more questions to be answered in another experimental system, which involves schizophrenic patients. Its future being undecided, it remains to be seen whether model psychosis research will produce what its practitioners have promised—insights into the neurobiology of schizophrenia and the development of better antipsychotics.[17]

16 A similar argument can be found in Luhmann (1999: 177f.).

17 As Mark Geyer pointed out to me, so far at least one antipsychotic has come out of model psychosis research: risperidone. Its forerunner, pipamperone, and possibly risperidone as well, were found by screening for drugs that would block the effects of both amphetamines and tryptamines such as LSD. Pipamperone was discovered in the Janssen laboratories in 1961, risperidone in 1984 (Healy, 2002: 251–4).

In any case, it is a pragmatist view of models that informs the concept of model psychoses in contemporary biological psychiatry. Being a form of scientific representation that has broken with realism, the hallucinogen model of psychosis has become almost as modernist as Magritte's painting. From this perspective, both the unreserved equation of the effects of hallucinogens with schizophrenia, as well as the outright rejection of the use of hallucinogenic drugs to model psychoses, miss the point. But it might well be in the nature of things that the hallucinogen model has often been misperceived.

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