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Focus on psychosis

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The concept of psychosis has been shaped by traditions in the concepts of mental disorders during the last 170 years. The term “psychosis” still lacks a unified definition, but denotes a clinical construct composed of several symptoms. Delusions, hallucinations, and thought disorders are the core clinical features. The search for a common denominator of psychotic symptoms points toward combinations of neuropsychological mechanisms resulting in reality distortion. To advance the elucidation of the causes and the pathophysiology of the symptoms of psychosis, a deconstruction of the term into its component symptoms is therefore warranted. Current research is dealing with the delineation from “normality,” the genetic underpinnings, and the causes and pathophysiology of the symptoms of psychosis.

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Introduction

Psychosis is a clinical syndrome composed of several symptoms. Delusions, hallucinations, and thought disorder may be regarded as core clinical features. A “nosology” of psychosis would need to be based on the knowledge of the causes and pathophysiology of these “psychotic” symptoms.¹ Psychosis is a clinical syndrome, not a nosological entity. The history of the term will be briefly described, followed by a description of its use in the current classification systems for mental disorders and a discussion on the necessity to deconstruct the term, along with the challenges and future prospects for psychosis research.

Historical aspects

The term “psychosis” has been used for about 170 years, and has evolved to reflect the scientific and social contexts of the respective times.² It was first used by the Austrian medical doctor Ernst von Feuchtersleben, who used the term in a textbook published in 1845.³ This reflected the current idea, of the time, of mental disorders being diseases of the mind (*Geisteskrankheiten* or *Seelenstörungen* in German), which von Feuchtersleben thought was too narrow and did not convey the idea that it was the interaction between the mind and brain that caused mental disorders. A later position, strengthening the concept of mental disorders as disorders of the brain, was introduced by Griesinger in 1845.⁴ The term “psy-

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chosis” was soon used by others, and a long and intricate history of its meaning ensued.^{5,6} In the late 19th century, the term was used widely and subdivided as exemplified by Wernicke’s distinction between “somatopsychoses” (affecting the consciousness of one’s own body), “autopsychoses” (affecting the consciousness of one’s personality), and “allopsychoses” (affecting the consciousness of the outside world).⁷ While such subdistinctions were the first indication that the term “psychosis” was not a unitary principle, but needed to be deconstructed into its component symptoms, these terms did not gain widespread acceptance. More importantly, Kraepelin’s dichotomy of psychosis into “dementia praecox” and “manic-depressive insanity” became the rule of the day, and the definition of the several dimensions of psychosis became the center of research in the early and mid-20th century. The concept of Jaspers’ “layers” of mental disorders⁸ also comes into play here, in that Jaspers hypothesized that neurotic, endogenous, and organic (exogenous) mental disorders reflected three different layers of mental disorders, in which psychotic symptoms could be found on both the “endogenous” and “organic (exogenous)” levels. The loss of reality underlying hallucinations and delusions became important, and the term “psychosis” has been used variably to denote a core syndrome of hallucinations, delusions, and disordered thinking, or in a wider sense, to encompass all severe mental disorders. On the background of such clinical diversity and variability, Schneider introduced a ranking of psychotic symptomatology, bringing into the discussion the notion that when diagnosing and classifying mental disorders, some psychotic symptoms may be more important than others.⁹

In today’s definition, the characteristic symptoms of psychosis are related to the degree of severity (with psychosis being the severe form of mental disorders), lack of insight, communication disorders, lack of comprehensibility of the symptoms, and reduced social adaptation.¹⁰

Current use of the term “psychosis” in the classification systems of mental disorders

Classifications of mental disorders and the necessary definitions of the clinical symptoms of mental disorders are mainly based on scientific evidence and aspects of practical utility. While drawing the line between “disorder” and “normality” is an important aspect of such

classification systems and symptom definitions, questions regarding the validity of the concepts of mental disorders come into play, as well as the quest for defining disease entities. This reflects etiopathological or pathophysiological insights, lending credibility to a concept of psychosis due to valid constructs. In a seminal paper, Robins and Guze¹¹ inspired the search for a psychiatric nosology based on etiology and pathophysiology.

Psychosis is conceptualized as a composition of clinically observable features. It is a clinical syndrome composed of various symptoms. The rationale is that, while there are some insights into the etiopathology and pathophysiology of psychotic symptoms, we cannot yet determine the exact mechanisms that are at work in individual cases of psychotic clinical manifestations. Thus, psychosis is still defined by the clinical picture and not by laboratory, genetic, or neuroimaging investigations. The set of symptoms used for a definition should be clearly observable, should be typical of psychosis, and should help to delineate psychotic states from other syndromes and “normality.” Of note, the degree to which these symptoms affect everyday functions should not be a part of the definition of psychosis—the presence of the necessary symptoms should suffice to diagnose a “psychosis” on a level of clinical observation.

Table 1 provides an overview of psychotic disorder groups from the American *Diagnostic and Statistical Manual of Mental Disorders (DSM)-5*.¹² The introductory text states that psychotic disorders are defined by abnormalities of one, or more, of five domains: delusions, hallucinations, disorganized thinking (speech), grossly disorganized or abnormal motor behavior (including catatonia), and negative symptoms. Note that a formal definition of “psychosis” is not given in the glossary of the *DSM-5*; only “psychotic features” are defined (“Features characterized by delusions, hallucinations, and formal thought disorder”¹²) and “psychoticism” as a feature of personality disorders (“Exhibiting a wide range of culturally incongruent odd, eccentric or unusual behaviors and cognitions, including both process [eg, perception and dissociation] and content [eg, beliefs]”). Psychoticism is one of the five broad personality trait domains defined in Section III, ‘Alternative *DSM-5* Model for Personality Disorders.’¹² At the time of writing, there was only an initial beta version of the *International Classification of Diseases (ICD)-11* online, but not the final version. *ICD-10* had no definition of the term “psychosis.”

It is evident that the main differences in metastructure occur for the following: (i) brief psychotic disorders, for which *DSM-5* has a special category; (ii) schizotypal disorder, which is classified as a personality disorder in *DSM-5*; and (iii) secondary psychotic disorders, which are grouped together with the primary psychotic disorders in *DSM-5*, but not ICD. Both classification systems also include other mental disorders, in which psychosis may occur, like states of delirium or mood disorders with psychotic features. Both classification systems keep psychotic syndromes in mood disorders separate from the “schizophrenia spectrum” (*DSM-5* terminology) or the group of “schizophrenia and other primary psychotic

disorders” (*ICD-11*). Ostergaard et al¹³ have reviewed the evidence for, and against, separating psychotic depression from the other psychotic disorders, as well as its status compared with the affective disorders, and have made suggestions for the diagnostic criteria of psychotic depression in *ICD-11* as part of the mood disorders.

In the process of developing *DSM-5*, a working group by the American Psychiatric Association on Psychotic Disorders reviewed the available evidence for regrouping the psychotic disorders. The group did acknowledge that the previous *DSM-IV* grouping had been based on tradition and shared psychopathology, and that the evidence for adding bipolar disorder was, at best, modest, while the evidence for including schizotypal personality disorder was stronger, but that the absence of frank psychosis in schizotypal personality disorder posed a conceptual problem. No decisive evidence for clustering psychotic disorders based on etiology was identified.¹⁴

DSM-5 still uses a categorical classification of psychotic mental disorders since the working group found that “the research needed to establish a new nosology of equal or greater validity is lacking.”¹⁵ Details of the proposals for *ICD-11* are provided in refs 16 and 17.

Neither *DSM-5* nor *ICD-11* opted to use an “attenuated psychosis syndrome” as a full diagnostic disease entity. *DSM-5* has defined such a syndrome as a clinical condition warranting more research, and the clinical criteria state that it is a syndrome characterized by psychosis-like symptoms below a threshold for full psychosis.¹⁸ This implies two nosological conundrums, in that “psychosis-like” as compared with “psychosis” is not defined, and it is unclear how a “threshold” for “full psychosis” can be operationalized. In *DSM-5*, it is suggested to include that the symptoms are “less severe and more transient,” and “insight is relatively maintained.” *DSM-5* emphasizes that functional impairment must have occurred. *ICD-11* is still in the process of developing its version of this subclinical state. *DSM-5* and *ICD-11* are moving toward harmonization (eg, the course specifiers of the psychotic disorders), but major differences will remain (eg, the time criterion of schizophrenia or the concept of schizoaffective disorder).¹⁶

Deconstruction of the construct “psychosis”

The composition of psychosis of several symptoms has led to the suggestion of deconstructing the term accord-

<i>DSM-5</i>	<i>ICD-11</i>
Schizophrenia spectrum and other psychotic disorders	Schizophrenia and other primary psychotic disorders
Schizotypal (personality) disorder	Schizotypal disorder
Delusional disorder	Delusional disorder
Brief psychotic disorder	Acute and transient psychotic disorder
Schizophreniform disorder	
Schizophrenia	Schizophrenia
Schizoaffective disorder	Schizoaffective disorder
Substance/medication-induced psychotic disorder	(To be listed in <i>ICD-11</i> among the substance-related mental disorders)
Psychotic disorder due to another medical condition	(To be listed in <i>ICD-11</i> among the organic mental disorders)
Catatonia associated with another mental disorder (catatonia specifier)	
Catatonic disorder due to another medical condition	
Unspecified catatonia	
Other specified schizophrenia spectrum and other psychotic disorders	Other specified schizophrenia and other primary psychotic disorders
Unspecified schizophrenia spectrum and other psychotic disorders	Schizophrenia and other primary psychotic disorders, unspecified

Table I. Psychotic disorders in *DSM-5* (published in 2013) and *ICD-11* (proposed revision as of September 2014). *DSM*, *Diagnostic and Statistical Manual of Mental Disorders*; *ICD*, *International Classification of Diseases*

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ing to its component symptoms.¹⁹⁻²¹ Factor analyses of the symptoms of psychosis in severe mental disorders, like schizophrenia, usually lead to a five-factor solution comprising hallucinations, delusions, disorganization, excitement, and emotional distress.²² If psychotic symptoms in the general population are taken into account, depressive and manic symptoms also come into play, reflecting the occurrence of the core clinical syndrome of psychosis in affective and other mental disorders.²³ Potuzak et al, after reviewing the available studies on the dimensional structure of psychosis, latent class analyses, and factor analyses, came to the conclusion that there is relatively consistent evidence on appropriate categories and dimensions for characterizing psychosis²⁴: the majority of the studies showed that either four or five dimensions describe psychosis, with positive, negative, disorganization, and affective symptom dimensions most frequently reported. Similarly, studies showed that the distinction between affective and nonaffective psychotic disorders still has validity and that the symptoms of psychotic disorders are rather stable clinical features when group analyses are carried out over longer observation periods of several years.²⁵ Importantly, in the early stages of disease development (ie, prodromal stages), affective disorders and schizophrenia are similar with dominating affective symptoms, but the occurrence of positive symptoms (eg, hallucinations or delusions) usually sets the mark for differentiation between affective disorders and schizophrenia.²⁶

A cluster of clinical symptoms encompassing, in a number of possible compositions of symptoms in individual patients, the psychopathologic domains of delusions, hallucinations, and disorganized thinking supplemented by affective domains is the core of psychosis. This notion is supported by the factor analysis results and the finding that these symptoms are characteristic of psychosis across traditional classificatory boundaries. They occur in different mental disorders and there is a considerable overlap between clinical presentations in different mental disorders, although there are symptoms that occur more often in schizophrenia compared with affective disorders with psychotic symptoms, for example.²⁷ This may indicate that the causes and pathomechanisms of psychotic symptoms in affective disorders are different from schizophrenia and related disorders. However, studies are lacking that address the question about the overlap frequency of symptom domains of the psychosis syndrome (eg, hallucinations,

disorganized thinking, or delusions) in individual patients, and about whether these show specific patterns of variation over time. The triad is not necessarily present in all patients, as is shown by disorders like delusional disorders. Of note, the clinical psychosis dimensions, such as “delusions” or “hallucinations,” need to be subdivided as they are composed of individual symptoms and associated latent factors.²⁸ Attempts are now under way to subdivide the three core psychopathological domains of psychosis even further, indicating that they may be “mixed bags” of symptoms with different etiopathogenesis, complicating the picture of “psychosis” even further.²⁹

Another unresolved issue is the question of the temporal variability of the psychotic symptoms in individuals. This leads to a very complex clinical situation: while there is a distinct “psychotic syndrome” of hallucinations, delusions, and disorganized thinking, the clinical appearance of “psychotic symptoms” may intraindividually vary greatly over time. This leads to the necessity of group analyses, which by their nature, limit the usefulness for determining the causes and pathophysiology of the symptoms in individual patients.

Future challenges for psychosis research

In the future, some major steps remain for the field of psychosis research. First, the causes and etiopathogenesis of the symptoms of psychosis need to be defined. Second, a succinct, clinically useful, and internationally harmonized definition of “psychosis” needs to be provided. Such a definition should also provide operationalized clinical criteria. Research into the etiopathogenesis and pathophysiology will benefit from harmonized definitions using research into the essential components of psychosis, which would most likely include delusions and hallucinations.

Drugs, substances of abuse and their withdrawal, or organic brain disorders (either primary brain disorders or secondary brain disorders that are found in general somatic disorders) may lead to psychosis in any person who may be exposed to these conditions. There has been progress in elucidating the pathophysiology of psychotic symptoms, such as delusions and hallucinations, and one of the new “organic” aspects is that neuronal auto-antibodies have been found to be associated with psychoses.³⁰ This puts the argument of shared biomarkers into a new light, since there is now a small percentage

of persons, among all persons with a psychotic disorder, who carry these autoantibodies. Another recent trend in psychosis research relates to the fact that some neurobiological signs are only detectable using sophisticated instrumentation and experimental paradigms in group analyses because the observed alterations of brain circuits are very small and prone to interindividual variation. For example, resting network alterations have been described in schizophrenia, which may help bridge the gap between minor structural brain alterations in patients with schizophrenia, but major disturbances of brain functions such as in perception and thinking. Currently, theories are being developed to conceptually link the areas of measurable neurobiological alterations and psychotic phenomenology.³¹ It seems unlikely that “neural signatures” of psychosis can be expected to be simple and straightforward. On the contrary, changes are manifold and often subtle, they are detectable with sufficient statistical significance based on group analyses, but hardly on an individual level, and they overlap boundaries of traditional *ICD-10* or *DSM-5* mental disorder categories. Investigations into the genetic underpinnings of psychotic disorders have also shown a bewildering number of genetic alterations, affecting a wide variety of biological pathways^{32,33} and a rather large overlap of different mental disorders. Studying distinct symptom dimensions of psychosis, even in large-scale genetic analyses, did not result in clear associations of specific genes with specific clinical dimensions of psychosis.³⁴ This genetic research, together with the previously mentioned clinical-course observations in psychotic disorders, supports the notion that psychotic clinical phenomena are spanning traditional classificatory boundaries and may indeed share etiopathology and pathophysiology across diagnostic borders.³⁵

The National Institute of Mental Health (NIMH) Research Domain Criteria (RDoC) initiative is following the path of putting symptoms, syndromes, and neurobiological signatures into the conceptual center of research, thus using the “deconstructing” approach.³⁶ Conceptual challenges arise because it remains to be seen whether identifying underlying neurocircuits will lead to new nosological definitions, and how the other aspects of the etiopathogenesis (eg, social and environmental factors) will be incorporated. There are probably a vast number of potential individual combinations of relevant factors leading to the clinical picture of psychosis. An important conceptual issue for RDoC

to address is how biological predispositions lead to symptoms of psychosis, which is only one of the conceptual and methodological challenges for the RDoC initiative.³⁷ In the long term, it would be desirable to use additional investigations from the fields of neuroimaging, psychophysiology, and genetics to reclassify psychosis into neurobiologically based subcategories of signs and symptoms. Research regarding the association of the symptoms of psychosis with structural or functional brain factors is just beginning (see below), lending some insight into differential associations of some psychotic symptoms with cortical thickness measures, which are, however, not sufficiently distinct on an individual level to provide a novel direction for “objectivating” and replacing clinical assessments with structural brain measurements.³⁸ Taken together, these findings seem to indicate that the symptoms of psychosis may find neurobiological explanations, but the road to achieving this aim is still long.³⁹ One of the issues to address is whether a specific bias of reality testing and the resulting reality distortion could be a common denominator of psychosis, with some evidence supporting the notion that impaired reality testing is found in several psychotic disorders and may be further deconstructed into refined neuropsychological dysfunctions.^{40,41} Psychological constructs associated with this model would be impaired source monitoring, increased proneness to jumping to conclusions and jumping to perceptions, and aberrant salience of irrelevant information, for which evidence from studies is available.⁴²⁻⁴⁶ The jumping-to-conclusions mechanism is also associated with other factors in patients with schizophrenia (eg, impairment of working memory),⁴⁷ while there is some evidence indicating that alterations of dopamine neurotransmission are involved in the aberrant salience dysfunction.⁴⁸ Based on these and other findings, recent theories propose that several dysfunctional brain networks interact in schizophrenia, including the salience network, executive network, and default resting state network.⁴⁹ Such neuropsychological and neurophysiological constructs and other factors (eg, genetic factors), could then be part of the endophenotype assessment battery of psychotic disorders, which could result from such research.⁵⁰ Endophenotypes are quantitative, heritable, trait-related deficits typically measured with laboratory tests including neuropsychological tests, which could be used to detect the underlying impairments of reality testing in psychotic disorders. Delineating and defining

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assessments will be part of the RDoC approach, as was recently shown for hallucinations.^{51,52}

Pending the results of such sophisticated analyses and ensuing revelations of putative highly intricate etiopathogenetic mechanisms, psychosis will remain a clinical description of a set of core symptoms, which can be detected by psychopathological investigations. Notably, this concept should be regarded philosophically as a “realistic” concept, which entails that the conceptual scheme mirrors the real world.⁵³ This means that psychosis is not a social or theoretical construct, but that psychosis is observable—in the world outside theories and concepts. As Malmgren et al put it, “Our concepts are formed while we are interacting with these natural phenomena.”⁵³ The border toward normality and questions about the early detection of psychosis emerge as essential critical issues, which are, however, an issue for all mental disorders and not just psychosis.⁵⁴

As to the early detection of psychotic disorders, it is currently clear that many psychotic disorders have a long period in which “subdiagnostic” or “subthreshold” symptoms occur and in which psychosocial interventions may be helpful to prevent the progression toward schizophrenia, for example.⁵⁵ Another aspect is that even after frank psychotic symptoms have occurred, the duration until appropriate treatment is initiated is very long, but a long duration of untreated psychosis implies a less favorable prognosis, although other factors (eg, involvement of cognition) are also important for predicting functional outcomes.⁵⁶

Another aspect is that there are symptoms of psychosis (or “psychosis-like” experiences), mostly of a fleeting nature in the population, leading to the question of the “border toward normality.” Over the lifespan of an individual affected by such symptoms, these are sometimes followed by progression to a mental disorder, but the symptoms usually subside spontaneously. The transition from “psychosis-like” experiences in otherwise healthy adolescents to psychosis is at a low rate of approximately 0.56% per year in persons with such “psychosis-like experiences,” which is, however, greatly increased compared with persons without such experiences (0.16% per year).⁵⁷ Also, such periods may be due to identifiable and treatable or preventable clinical situations, such as sleep problems, sensory deprivation, intoxicating effects of drugs or substances of abuse, states of withdrawal from drugs or substances of abuse, or they may be associated with somatic dis-

orders including brain disorders (see van Gastel et al⁵⁸ on the association with cannabis use). Such psychotic symptoms and psychosis-like experiences may signal hitherto unidentified mental disorders.⁵⁹

In the unselected, general population, as many as 17% endorse having had lifetime psychotic symptoms (as defined by the Composite International Diagnostic Interview [CIDI]), but only 2% to 5% have ever had a diagnosis of a psychotic disorder. In such studies, there are some associations (eg, for delusions and female sex, and hallucinations and male sex), but there is considerable overlap between associated factors and symptom profiles.⁶⁰ Also, in such studies, a range of mental disorders (eg, substance addiction or affective disorders), emerge as psychosis-associated, besides the “primary” psychotic disorders (eg, schizophrenia). Research in adolescents who are “at risk” of psychosis indicate that the overlap of these symptom groups and the ensuing pattern of psychotic symptoms may become an indicator of progression to psychotic disorders, although research into this question is still in its infancy.⁶¹ How can “truly” psychotic symptoms be differentiated from “psychotic-like experiences,” “unusual subjective experiences,” and similar experiences, and what is their prospective value for predicting the future occurrence of mental disorders in general and psychotic disorders in particular?⁶² Obviously, further research is necessary to delineate the experiences of psychotic symptoms from those of a “psychosis-like” nature, and such psychopathological research is just beginning.⁶³ Given the high frequency of such experiences in the general population, and the impairments and suffering associated with them if they progress, there is a clear clinical need to address these questions, which may have consequences for the nosological status of “mild” or “attenuated” psychotic experiences in the general population.

Future research in psychosis: where is it heading?

Three avenues of progress are currently shaping the field. First, there is now stereoelectroencephalographic evidence derived from studies with intracranial electrodes during epilepsy surgery showing that some symptoms of psychosis may result from stimulation in different brain areas, and that complex brain networks are obviously involved. Interestingly, there seems to be considerable overlap in the pathophysiology of hallu-

cinations and delusions using such technologies, which has prompted a debate on whether the “psychiatric” distinction between hallucinations and delusions was warranted.⁶⁴ The question arises whether the same principles apply to nonictal psychosis.

A second technique is the use of neuroimaging methods to identify areas of the brain involved in the pathophysiology of hallucinations and delusions. While this research is ongoing, it seems clear that there are no single brain regions that are more decisive, but that complex network disturbances occur in the context of these phenomena and that many combinations of functional alterations may be detectable.⁶⁵ The question is whether the symptoms of “primary” (or “endogenous”) psychotic disorders will prove to have similar pathophysiology compared with those in other brain disorders (eg, Alzheimer’s disease).⁶⁶ The genetics of psychotic manifestations in Alzheimer’s disease show some overlap with schizophrenia genetics, but both fields of research have so far yielded a bewildering array of associations with a multitude of genes. It seems impossible to pinpoint individual genes in individual cases.⁶⁷

A third approach utilizes novel methods of brain network analyses (“connectome”)⁶⁸ and the results are preliminary and complex, and have not yet provided distinguishing landmarks for analysis suitable for clinical practice. However, research advances in the brain network analysis of the symptoms of psychosis (eg, relevant neurotransmitter systems including γ -aminobutyric acid [GABA] and glutamate) as well as proteomic approaches combined with genomic approaches are beginning to reshape the concept and therapeutic approaches of psychotic disorders.^{69,70} New concepts of psychosis are emerging as the result of the neurobiological research progress, including the theory of dopamine hypersensitivity caused by a range of pathological insults that may be a common denominator, with the concept also taking into account brain reactions in the different dopamine pathways (both intracellular and intercellular) and the counterreactions by the same pathways or due to altered interactions among each other.⁷¹ Today, alterations of the dopamine system and their interactions with other neurotransmitter systems are viewed not as the causes, but rather as the consequences of a cascade of events in the etiopathogenesis of psychosis.⁷² They seem to represent a common final pathway, amenable to treatment with antipsychotic drugs across traditional diagnostic boundar-

ies of mental disorders. Gene-environment interactions are another important aspect here as it appears highly likely that not only do “endogenous” processes play a role, but also exogenous factors (eg, environmental factors) codetermine the timing, type, and course of psychosis.^{73,74} However, large-scale epidemiological studies indicate that the gene-environment-symptom pathway is complex and highly variable between individuals, leading to weak associations between these factors, even in large-scale studies.⁷⁵ Now there are attempts to associate specific developmental insults with specific symptoms or specific disease trajectories of psychotic disorders, but this research is just beginning.⁷⁶⁻⁷⁸ Once psychotic disorders have developed, studies in patients with treatment-refractory vs nonrefractory psychotic disorders show that the “old” differentiation between schizophrenia, bipolar disorder, and schizoaffective disorder still has prognostic validity. These classes of mental disorders are associated with differential treatment responses in specific clinical domains of psychosis,⁷⁹ and they emerge in latent class analyses in cohorts of patients with mental disorders and healthy controls.⁸⁰ These findings indicate that there may be differential pathways into these specific symptoms, which need to be unraveled by future research in more detail. While this research has a rather long-time perspective between the insult and ensuing symptoms, research is now also addressing fluctuations of psychotic symptoms on a micro-timescale of hours. Initial results indicate that such assessments are feasible, may lend insight into the complex array of environmental or affective factors influencing the clinical presentation of psychosis, and indicate that such momentary states are the basic units of psychosis.^{81,82,83} The expected progress in these areas of (neuro) systems-oriented research will clearly bear on the concept of psychosis and the methodology of elucidating the etiopathogenesis of mental disorders in general.⁸⁴

Taken together, the etiopathogenesis of the symptoms of psychosis is complex and involves a number of environmental and endogenous factors (eg, genetic and neurodevelopmental factors), which interact in an intricate manner leading to a range of structural and functional adaptive or maladaptive responses of the brain.⁸⁵ Novel research approaches based on the deconstruction of the psychosis syndrome into its symptoms hold promise for unraveling the causes and pathophysiology of these symptoms in the future.

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Conclusions

Psychosis is a clinical syndrome composed of several symptoms. It is not a nosological entity. Symptoms of psychosis occur in a wide range of mental disorders and show a high degree of interindividual variability between persons with different mental disorders, and a high degree of intraindividual variability over time. Symptoms of psychosis are usually embedded in the wider clinical picture of the mental disorder, which may include symptoms of mania and depression. The elucidation of the symptoms of psychosis by drugs or brain disorders indicates that every person may experience symptoms of psychosis. While the concept and definition of psychosis are characterized by the core clinical symptoms of delusions, hallucinations, and disorganized thinking, it is most likely that these symptoms are common final outcomes of a range of different causes and etiopathogenetic pathways, which may all lead to a similar clinical picture. As Kraepelin

put it, the human brain only has a limited number of reaction types (a concept relating to Bonhoeffer's reaction types)⁸⁶ in the face of etiopathogenic insults.⁸⁷ The clinical efficacy of antipsychotic drugs against the symptoms of psychosis, irrespective of the mental disorder, indicates that such final common pathways play a role. The symptoms of psychosis are a common clinical result of a number of causes and pathomechanisms. Therefore, the need arises to deconstruct the construct into its clinical dimensions with a view to identifying the causes and pathomechanisms of each of the symptoms of psychosis. There may be shared causes and pathomechanisms, since the symptoms of psychosis commonly occur together, which seem to converge on some common final pathways of the brain, leading to the similar efficacy of antipsychotic drugs in different mental disorders where these symptoms occur. Future challenges are to identify the causative and pathophysiological components, and their interplay in individual cases. □

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Foco en las psicosis

Durante los últimos 170 años el concepto de psicosis se ha configurado a través de las tradiciones de los conceptos sobre los trastornos mentales. El término “psicosis” todavía carece de una definición unificada, pero da cuenta de un constructo clínico compuesto por varios síntomas. Los delirios, alucinaciones y trastornos del pensar constituyen las principales características clínicas. La búsqueda de un denominador común de los síntomas psicóticos apunta hacia combinaciones de mecanismos neuropsicológicos que se traducen en una distorsión de la realidad. Para avanzar en la clarificación de las causas y la fisiopatología de los síntomas de la psicosis se justifica una deconstrucción del término en sus síntomas que lo componen. La investigación actual está abordando la descripción a partir de la “normalidad”, las bases genéticas y, las causas y la fisiopatología de los síntomas de la psicosis.

Cap sur la psychose

Ces 170 dernières années, le concept de psychose a été modelé par la tradition dans la notion de troubles mentaux. Le terme de « psychose » manque encore d’une définition unifiée, mais reflète une construction clinique composée de plusieurs symptômes. Les caractéristiques cliniques de fond sont le délire, les hallucinations et les troubles de la pensée. La recherche d’un dénominateur commun des symptômes psychotiques suggère une association de mécanismes neuropsychologiques aboutissant à une distorsion de la réalité. Déconstruire le terme en ses symptômes constitutifs est donc nécessaire pour progresser dans la compréhension des causes et de la physiopathologie des symptômes de la psychose. La recherche actuelle traite de la délimitation de la « normalité », des fondements génétiques et des causes et de la physiopathologie des symptômes de psychose.

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