The Diagnosis of Schizophrenia: Old Wine in New Bottles

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ABSTRACT

Diagnosing schizophrenia has been problematic since the earliest clinical descriptions of the disorder, and the existence of basic disagreements in the concept is reflected by the large number of competing diagnostic systems that have been proposed. Given that the ultimate goal of any diagnostic system is to provide insights into the etiology, pathophysiology and treatment of the disorder, it is essential to examine the accuracy of the diagnostic construct. In this report, we analyze a number of clinical models of schizophrenia ranging from historical to present ones. It is concluded that empirical data fit better with a dimensional view of schizophrenia than with a categorical one, and given the continuous distribution of the schizophrenia-related variables, it may be arbitrary where cutpoints are made between schizophrenic and non-schizophrenic psychoses.
Key words: schizophrenia, psychosis, diagnosis, dimensional models, categorical models

RESUMEN

El diagnóstico de esquizofrenia ha sido problemático desde las primeras descripciones de la enfermedad, y la existencia de numerosos criterios diagnósticos es la consecuencia de desacuerdos fundamentales en la definición del trastorno. Dado que la finalidad última del diagnóstico es arrojar luz sobre la etiología, patología y tratamiento del trastorno, es esencial estudiar la validez del diagnóstico. A este respecto, en el presente estudio analizamos los modelos clínicos de esquizofrenia desde aquellos con importancia histórica a los actuales. Los datos empíricos existentes apoyan un modelo dimensional de la esquizofrenia, y dado que las variables clínicas asociadas a la esquizofrenia tienen una distribución continua en el espectro de las psicosis, los límites establecidos por los diagnósticos categoriales entre psicosis esquizofrénicas y no esquizofrénicas son arbitrarios.
Palabras clave: esquizofrenia, psicosis, diagnóstico, modelos dimensionales, modelos categoriales.

It has been shown that heterogeneity in schizophrenia is best described at three levels: phenomenological, pathophysiological, and etiological (Tsuang *et al.*, 1990). The heterogeneity issue in schizophrenia has been largely acknowledged as reflected by the term 'schizophrenias' coined by Bleuler (1911). With this term Bleuler intended mainly to describe heterogeneity at the clinical level. Afterwards, heterogeneity in etiology and pathophysiology has also been largely acknowledged. It is unreasonable

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to expect that patients who are heterogeneous not only in their symptoms, but also in their course and outcome, share a common cause or pathological mechanism. Much effort has been made in linking levels of heterogeneity, particularly between pathophysiology and phenomenology. However, the extent to which the clinical, pathophysiological and etiological levels are interrelated is still largely unknown. Progress in understanding the disorder may have been hampered by the heterogeneous groups -at clinical, etiological and pathological levels- of patients whom researchers have been required to study under the name of schizophrenia.

In absence of available biological markers for diagnosing, classifying, and subtyping schizophrenia, descriptive psychopathology continues to be the basis for diagnosis and treatment. However, the study of phenomenology and nosology is not an end in itself. The main goal of descriptive psychopathology and nosology is to identify a method or methods for classifying disorders which are ultimately related to pathophysiological mechanisms and etiology. The main hypothesis held in this report is that as long as we are not able to disentangle the heterogeneity question at the clinical level, it is not likely that heterogeneity at the etiological and pathophysiological levels can be resolved.

Schizophrenia is an evolving concept and along the last 100 years a number of diagnostic systems (i.e. clinical models) have been proposed. While the description of symptoms and signs of the disorder has remained basically unchanged over the years, the way in which authors have articulated the varied phenomenological manifestations has been very different. The richness of the psychopathology of schizophrenia, which Kraepelin (1919) and Bleuler (1911) described so vividly, appears to be its main weakness. Ideally, a model -in this case a clinical model- should have the following characteristics: i) it should be a theoretical construct of symptoms, this is, it should underlie a hypothesis about how the symptoms arise; ii) the hypothetical assumptions of the model should be clearly formulated in order to be operationalized and tested; iii) the model should have heuristic value, i.e. it should be able to organize information and reduce uncertainty; and iv), the model should have predictive validity.

Given that the ultimate goal of any diagnostic system is to provide insights into the etiology, pathophysiology and treatment of the disorder, it is essential to examine the accuracy of the diagnostic construct. In this report, we will analyze a number of clinical models of schizophrenia ranging from historical to present ones. This analysis does not seek to be a detailed review of models, but a critical analysis of the most significative or influential ones.

Basic Premises of the Diagnostics Systems

Diagnosing schizophrenia has been problematic since the earliest clinical descriptions of the disorder, and the existence of basic disagreements in the concept is reflected by the large number of competing diagnostic systems that have been proposed. The magnitude of the problem is well illustrated by the finding that diagnostic systems may vary as many as sevenfold in their rates of diagnosing the disorder (Endicott *et al.*, 1982). Furthermore, diagnostic systems of schizophrenia have been criticized on the

basis of their unestablished construct validity and arbitrariness (Fenton *et al.*, 1981). These problems have been interpreted by some authors as the demonstration of the existence of something profoundly wrong in the schizophrenia concept (Brockington, 1992).

Although it is generally accepted that attempts to define schizophrenia ultimately refer either to Kraepelin, Bleuler or Schneider, divergences in diagnostic systems cannot, however, simply be explained by the adherence to one of these three diagnostic approaches. A more careful analysis reveals that all diagnostic schemes, including those claiming to be based solely on descriptive or pragmatic considerations, are actually based on a number of underlying assumptions that remain to be demonstrated. According to Berner *et al.* (1992) these assumptions are: (a) Bayle's nosological hypothesis stipulating that schizophrenia is a discrete disorder with specific cause(s) and mechanism(s); (b) Moebius's endogeny hypothesis asserting that schizophrenia is genetically determined; (c) Kraepelin's outcome principle involving that schizophrenia leads to deterioration; (d) Bleuler's pathogenic basic disturbance that states that some symptoms (i.e. thought disorganization) are the expression of a putative primary brain disturbance; (e) Jaspers's hierarchical principle stating that certain symptoms (i.e. 'schizophrenic' symptoms) do have diagnostic prominence over others (i.e. mood symptoms); and (f) Schneider's psychological principle stating that the bizarre character of delusions or hallucinations is disorder-specific.

Divergences in diagnostic schemes of schizophrenia depend upon the degree to which they take the aforementioned principles into consideration, the great variation in diagnostic systems (and therefore in their constituting features) being a expression of this. Beyond these theoretical considerations, two putative factors could also explain variability among schizophrenia definitions: the existence of different disorders within the schizophrenia construct, and the dimensional nature of the construct that hardly can be operationalized in terms of categorical definitions. In the first case, the different schizophrenia schemes (or clusters of them) would be the expression of the existence of several underlying discrete disorders, and in the later case, the different schizophrenia schemes would be, at least in part, the expression of setting different cutpoints to a dimensional construct.

Historical Models

The importance of taking into account historical models of schizophrenia is due to the fact that they continue to be the basis for describing and diagnosing the disorder. These models are very different from each other in terms of theoretical assumptions and hence diagnostic value casted on the symptoms having contributed in a varying degree to the modern definitions of the disorder.

When Kraepelin (1919) combined under the term 'dementia praecox' several clinical pictures, that had previously been considered as different disorders, he set the basis for the later debate about whether schizophrenia is either a unitary construct or a heterogeneous group of disorders. The germ of Kraepelin's idea of dementia praecox was the convergence of different clinical forms to a defect state. According to this author schizophrenia is characterized by a deteriorating course in which the *Verblödung*

-loss of affect and volition- is the main symptom. In current terms the disorder would be characterized by enduring primary negative symptoms (Carpenter *et al.*, 1998). The main theoretical implications of Kraepelin's model of schizophrenia were (a) a discrete disease entity, (b) a poor outcome, and (c) the negative symptoms are the most characteristic ones and give the unity character to the disorder.

Bleuler's (1911) conception of schizophrenia differs from that of Kraepelin's in three ways. First, he moved the point of gravity of the fundamental features of the disorder from the negative symptoms to the disorganization ones (i.e. the 'loss of association' in thought processes). Second, he expanded the limits of the disorder by including psychotic disorders with affective features (schizoaffective disorder) and a mild form of schizophrenia (schizophrenia simplex). Third, Bleuler did not include criteria of course or outcome and emphasized the cross-sectional diagnosis of the disorder.

Kurt Schneider (1958) described a number of disturbances of the experience, the first-rank symptoms (FRS), as characteristics of schizophrenia on the basis of their radical non-understandable character. According to this author, FRS do posses a typological (diagnostic) value and no hypothesis about their underlying etiopathogenic character was formulated. The FRS possess high clinical and diagnostic relevance as they have been implemented in all modern diagnostic criteria of schizophrenia.

Carl Schneider (1942), by applying the Hoche's concept of 'symptom complexes', took a radically different approach in explaining the clinical manifestations of schizophrenia. A symptom complex is defined as a group of symptoms which tend to run together, being supposed that they share some underlying mechanism. This author specifically described three symptom complexes in schizophrenia which are very similar in symptom composition to the modern concepts of psychosis, disorganization and negative syndromes (see below). The author believed that the symptom complexes tend to run either simultaneously or independently, have different prognostic value, may appear in disorders other than schizophrenia, are the expression of a disturbed normal psychological function, and have specific neurobiological representations. This conception implies a dimensional view of psychopathology, and Carl Schneider may, therefore, be considered as the forerunner of the modern dimensional approach to the phenomenology of schizophrenia.

The positive and negative symptoms models

The concept of positive and negative symptoms was developed in an attempt to integrate the various aspects (symptoms, pathophysiology, outcome) of schizophrenia. This concept was already implicit in Bleuler's distinction between fundamental and accessory symptoms, with most of the former corresponding to negative symptoms and most of the latter corresponding to positive symptoms. After Bleuler, the concept was used and developed by various authors and particularly by Strauss *et al.* (1974). These authors explicitly classified the positive and negative symptoms according to their clinical significance and differentiated negative symptoms from social dysfunction. With Crow (1980) positive and negative symptoms have become a major focus of attention in clinical and biological research. Crow posited that these symptoms are

associated with different pathological brain mechanisms, neurochemical for the positive symptoms and structural for the negative ones. Crow's powerful heuristic hypothesis has promoted ongoing research on phenomenology, biology, genetics, and treatment of schizophrenia. Andreasen developed the Scales for the Assessment of Positive and Negative Symptoms (SAPS and SANS) which have become the most popular instruments for assessing schizophrenic symptoms and described the first operationalized criteria for positive and negative schizophrenia (Andreasen & Olsen 1982).

Crow's and Andreasen's models differ significantly. Originally, according to Andreasen, the positive and negative symptoms represent a unique dimension with a bipolar character. According to Crow positive and negative symptoms define two types of schizophrenia. Subsequently this author modified his theory proposing that both groups of symptoms are semi-independent processes that can occur simultaneously (Crow, 1985). While the model by Strauss *et al.*, did not clarify whether it was a categorical or a dimensional one, both Crow's and Andreasen's models were categorical. The categorical positive-negative model was soon abandoned since it was evident that subtypes were not stable over time (Marneros et al., 1991) and that a substantial proportion of patients -if not the majority- had both types of symptoms conforming a disproportionate 'mixed' group (Peralta *et al.*, 1992). However, positive and negative symptoms have continued to be used as dimensional constructs supported by some external validity (Fenton & McGlashan, 1991; Peralta *et al.*, 1995).

Multidimensional models of pscychopathology

The concept of positive versus negative schizophrenia led to the development of rating scales to measure it, and afterwards, the study of their psychometric properties resulted in two important changes in the original concept: the shift from a categorical view of symptoms and syndromes to a dimensional one, and the change of a two-dimension conception into a multidimensional one. Factor-analytic studies of positive and negative symptoms have consistently demonstrated the existence of at least three factors or dimensional syndromes: psychosis, disorganization and negative, which form a multidimensional model of schizophrenic psychopathology. In terms of Andreasen's scales the psychosis dimension is made of delusions and hallucinations, the disorganization dimension comprises formal thought disorder, bizarre behavior and inappropriate affect, and the negative dimension consists of affective flattening, alogia, and avolition-apathy. This three-dimension approach closely corresponds with historical and categorical views of schizophrenia and has been included in the DSM-IV as an alternative approach to classify schizophrenic symptoms.

Despite the lack of evidence supporting the positive-negative dichotomy of schizophrenic symptoms and syndromes, some authors (Andreasen *et al.*, 1995) continue to posit that the positive-negative terminology is a valid one maintaining that features from the psychotic and disorganization dimensions are positive symptoms. This assertion has been contradicted by various studies (Peralta *et al.*, 1994; Brekke *et al.*, 1994; Dollfus & Everitt, 1998) showing that disorganization and negative dimensions are strongly correlated, thus challenging the view of disorganization as a positive dimension.

Both, the lack of factorial validity for the positive and negative symptoms, and the association of the disorganization dimension with the negative rather than with the positive dimension, should lead to abandon the positive-negative dichotomy of schizophrenic symptoms.

In the last years more complex multidimensional models have been reported. The validity of the distinction between negative and social dysfunction symptoms suggested by Strauss *et al.* (1974) has been empirically demonstrated and a four-syndrome model based on the positive and negative symptom scales comprising the dimensions of psychosis, disorganization, negative, and social dysfunction has been proposed (Peralta *et al.*, 1994; Dollfus & Everitt, 1998).

There is little agreement about the number of dimensions necessary for an adequate representation of the schizophrenic psychopathology, and views remain largely dependent on the rating scale employed (Peralta & Cuesta, 2001). For example, Kay & Sevy (1990) using the Positive And Negative Syndrome Scale (PANSS), suggest seven dimensions, although the consensus at this point is that just five factors -positive, negative, depressive, disorganization, and excitement- are the ones best representing the scale's factor structure (Lindenmayer *et al.*, 1994).

The positive and negative symptom rating scales by being the most used instruments for assessing clinical symptoms have severely limited the study of other clinical manifestations of schizophrenia, and have produced a sort of 'scotomas' -even not hemianopsia- in our view of the whole clinical picture of schizophrenic patients. Besides the well-established psychosis, disorganization, social dysfunction and negative dimensions, and the additional PANSS dimensions of excitement and depression, there are many other dimensions of psychopathology which are usually neglected. These are among others the dimensions of mania, lack of insight, subjective experiences, psychomotor (i.e. catatonic) and neurological (Peralta & Cuesta, 2001). The multidimensional model is even more complex if one considers that most of the psychopathological dimensions of schizophrenia can be further subdivided into more fine-grained dimensions conforming a hierarchical model of psychopathology ranging from high-order dimensions (i.e. positive, negative and affective) to low-order dimensions close to the symptom level (Cuesta & Peralta, 2001).

A question of great theoretical and clinical relevance is whether or not the dimensions described in schizophrenia are specific to the disorder. Studies examining this issue have found that the three-factor structure (psychosis, disorganization and negative) is also present in affective psychoses, schizophreniform disorder and in a mixed group of delusional, brief reactive and atypical psychoses (Peralta *et al.*, 1997). The implication of these findings is that 'schizophrenic' dimensions cut across the whole spectrum of psychotic disorders, and thus they should be considered dimensions of the psychotic illness rather than 'schizophrenic' dimensions. A further implication related to this lack of specificity is that clinical dimensions can be studied irrespective of diagnostic categories of psychotic disorders.

The diagnostic and statistical manual (DSM) model

The schizophrenia model derived from the successive DSM editions (particularly after the DSM-III edition) is the most influential one over the world, both in clinical practice and research. The main purpose of the DSM diagnostic system (like other consensus diagnostic systems) is to achieve a greater diagnostic reliability across clinicians and countries. This objective has been met to a great extent, but reliability does not equal validity. The DSM schizophrenia concept provide an oversimplified and incomplete view of the clinical picture leading to the assumption that we are confronted with a simple, clear and discrete disorder. This assumption is far away from the clinical reality. Compromise or consensus diagnosis in words of Berner *et al.*, 'suffer from all the imperfections inherent in any compromise: for reasons of general and psychiatric policy, conflicting positions and formulations had to be incorporated into each system often at the expense of clarity, theory and logic' (Berner *et al.*, 1992).

With the aim of obtaining a prototypical disease entity using an atheoretical and pragmatic approach, the DSM model has provided us with a mixture of clinical phenomena such as arbitrary inclusion, exclusion, and duration criteria lacking an underlying paradigm (Maj, 1998). Despite the relatively narrow schizophrenia concept conveyed by the DSM system, it has not served to clarify the conceptual and clinical heterogeneity of the disorder. As Berner *et al.* (1992) pointed out, while consensus diagnosis may be adequate for clinical practice and health statistics, they are inadequate for research as they tend to conceal alternative views of the disorder.

Current DSM schizophrenia is intended to be formulated on the basis of historical definitions, mainly those of Kraepelin, Bleuler and Kurt Schneider. Historical definitions, however, represent different conceptions of the disorder as they scarcely overlap. The concordance between the DSM concept and its historical antecedents is relatively modest (Peralta & Cuesta, 2000), suggesting that rather than incorporating the original paradigms the DSM contains residual features of them. As a consequence, DSM schizophrenia is concealing its historical roots. Historical definitions of schizophrenia continue to be the basis for powerful hypothesis about the disorder and deserve to be tested on their own against external validators including possible pathophysiological and etiological factors.

The categorical versus dimensional approach to diagnosis

In dealing with a categorical view of schizophrenia, the main question that arises is the delimitation of the schizophrenia concept itself. It is well established that there are not pathognomonic symptoms for schizophrenia (Pope & Lipinski, 1978), that no clear separation of prototypical psychoses can be made on the basis of clinical symptoms (Kendell & Brockington, 1980), and that the factor structure of symptoms breed true across psychoses (Peralta *et al.*, 1997). Diagnostic conventions impose boundaries on a continuum of 'schizophrenic' symptoms of varying prevalence, severity or duration. Whatever putative boundary one examines, the variation in the schizophrenia-related features is continuous. In other words, given the continuous distribution of the schizophrenia-related variables (Mying-Germeys *et al.*, 2003), it may be arbitrary where

cutpoints are made between schizophrenic and non-schizophrenic psychoses, and between psychotic and non-psychotic disorders. This does not mean that a categorical diagnosis of schizophrenia does not make sense at all, in fact it is necessary for the purposes of case identification and treatment. However, the categorical approach based on a unitary concept of schizophrenia may not represent the most useful paradigm on which to base research.

The absence of a gold standard to establish diagnostic validity, has led to the fact that current definitions of the disorder have been mainly based on arbitrary (either theoretical or compromise) grounds. An ideal way to resolve this question is to use alternative definitions of schizophrenia which can be applied to the same subject or population. This is known as the polydiagnostic approach to the classification of functional psychoses (Berner *et al.*, 1982; Berner & Katching, 1984). The polydiagnostic approach represents an interesting paradigm in psychiatric research which can contribute to the solution of controversies arising from both the lack of a clear definition of the boundaries of schizophrenia, and the heterogeneity of the disorder.

In opposition to categorical models which classify patients, dimensional models classify symptoms. This latter approach has many desirable characteristics for addressing the heterogeneity issue. The dimensional approach emphasizes quantitative gradations of psychopathology, both within- and between-subjects, rather than qualitative, discrete, all-or-none class distinctions. One of the most striking characteristics of the dimensional models is that, unlike the categorical ones, dimensions of psychopathology are not exclusive but complementary and additive. Consequently, information is not lost and external validity studies do not convey any concealment of information.

A dimensional schizophrenia construct is consistent with the interpretation that traditional diagnostic systems are the result both of drawing artificial boundaries on a dimensional construct and of emphasizing (or de-emphasizing) aspects of the construct. This view of schizophrenia is compatible with findings from several areas. From a statistical point of view, Grove (1991) compared two mathematical strategies (categorical and dimensional) for predicting a criterion variable and showed that over almost all of the parameter space encountered in psychopathology, dimensional prediction of the criterion was superior to taxon-mediated prediction. This finding has been corroborated by a number of recent studies (van Os *et al.*, 1999; Peralta *et al.*, 2002; Rosenman *et al.*, 2003) that have comparatively examined the predictive validity of dimensional and categorical models of psychosis and have consistently shown the superiority of the dimensional models over the categorical ones. On the other hand, a body of research (reviewed by van Os *et al.*, 1998) has accumulated suggesting that, within the field of psychotic disorders, a dimensional view of schizophrenia is consistent (or inversely, a categorical view is inconsistent) with findings stemming from different areas of research indicating a continuous variation in risk factors, symptoms, outcome and neuroimaging variables.

It should be acknowledged however, that likewise other psychiatric disorders, categorical and dimensional representations of schizophrenia, are not antagonistic but complementary (Strauss & Rochester, 1973; Millon, 1991), and that for categorical definitions different cutoff points may have different validity and utility. The main

point here is not whether the *disorder* is categorical o dimensional, but whether the *diagnosis* should be categorical or dimensional in order to yield the best clinical and research results (Kraemer *et al.*, 2003).

The polydiagnostic-multidimensional paradigm

With respect to the categorical versus dimensional argument, one false assumption is that the disorder is either categorical or dimensional. In a real sense, schizophrenia (and every mental disorder) is both categorical and dimensional, and the point here is to know in which cirscumstances one approach works better than the other.

Necessarily, approaches dealing with heterogeneity at the clinical level must take into account both, the lack of a clear delimitation of schizophrenia against other psychotic disorders, and the manifold manifestations of the disorder. The polydiagnostic approach deals mainly with the former problem, and the multidimensional approach with the latter. Combining the two strategies into a polydiagnostic-multidimensional approach seems to be a promising research method for analyzing the heterogeneity of schizophrenia. This approach represents a more comprehensive strategy than either the polydiagnostic or the multidimensional approach and seems to be a useful method for organizing and systematizing the varied clinical manifestations of schizophrenia as it integrates categorical and dimensional models into a unitary paradigm. Using this paradigm a given patient or group of patients may be assessed according to alternative diagnostic systems of schizophrenia together with quantitative psychopathological scales, and then diagnoses and psychopathological dimensions can be ralated to specific clinical or research questions.

Some authors have argued that the categorical and dimensional approaches often have different aims and answer different questions (Mojtabai & Rieder, 1998). The polydiagnostic-multidimensional paradigm by integrating both units of analysis should help to establish for which clinical or research questions the dimensional approach works better than the categorical approach and vice versa.

Conclusions

Clinical and etiopathological heterogeneity in schizophrenia has been recognized long ago, and the main objective of this paper has been to highlight how several competing models try to deal with the complex clinical manifestations of schizophrenia. While the description of symptoms and signs of schizophrenia has remained mainly unchanged over the years, the way in which authors have articulated their varied phenomenological manifestations has been very unequal, thus rendering different views of schizophrenia across periods and countries. The aim of achieving a clear-cut nosological entity for schizophrenia by means of the precise delimitation from either other psychotic disorders or non-psychotic conditions has not been met. Clinical models of schizophrenia (i.e. historical, the positive-negative dichotomy or the DSM model) have risen and fallen, and we still lack any definitive tool for organizing the complex phenomenological manifestations of the disorder. Acknowledging that schizophrenia is neither an entity

nor a unity, we should analyze its psychopathology through its elements, and search for the factors which determine each of them. In absence of compelling evidence for supporting either a categorical or a dimensional view of the disorder, it is necessary to integrate and empirically compare competing approaches. The use of a polydiagnostic approach on the one hand, and a multidimensional approach on the other (the polydiagnostic-multidimensional paradigm), seems to be a promising strategy to better understand the heterogeneity of schizophrenia. Any alternative to the current approaches must also demonstrate that has a greater predictive validity, since this factor, more than any other, is ultimately the one which determines the utility of a clinical model of schizophrenia

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