Biological, Life Course, and Cross-Cultural Studies All point Toward the Value of Dimensional and Developmental Ratings in the Classification of Psychosis

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The recent history of the classification of psychoses. For the categorical diagnosis of schizophrenia to be scientifically valid, it should define a syndrome with specific risk factors, psychopathology, treatment responses, and outcomes; clear symptom boundaries should separate it from other conditions such as the affective psychoses. That such a distinction could be made between “dementia praecox” and “manic depressive insanity” (schizophrenia and affective psychosis) has been fundamental to psychiatric classificatory systems since Kraepelin’s original proposal of the dichotomy in the 19th century. This is despite the fact that in 1920 Kraepelin came to doubt his own approach and suggested replacing his defining principle with a dimensional-hierarchical model more appropriate to the heterogeneity of clinical presentations. Furthermore, in spite of the theoretical distinction between schizophrenia and mood disorder with psychotic features, the practicalities of clinical life led to development of a less satisfactory intermediate category—schizoaffective disorder.

Attacks on the Concept of Schizophrenia

The 1960s saw a sustained attack on psychiatry from the so-called antipsychiatrists including R. D. Lang and Thomas Szasz, curiously both psychiatrists, who argued that psychiatric diagnoses such as schizophrenia were arbitrary categories that did not correspond to clinical reality. Then in the 1990s, more academically sophisticated criticism came from British clinical psychologists such as Richard Bentall and Mary Boyle who argued that a symptom-based approach was less stigmatizing and more appropriate from a therapeutic point of view. However, criticism did not just stem from outside orthodoxy psychiatry. Phenomenologists such as Brockington, biological researchers such as Crow, and epidemiologists such as Van Os have led a growing chorus of dissent from within the ranks of psychiatrists.
The Hope Promised by Operational Definitions

From the late 1960s onward, a number of competing operational diagnostic systems were proposed in an attempt to improve the reliability of psychiatric diagnosis for research purposes. These included Feighner’s, Taylor’s, Schneider’s, Langfeldt’s, Spitzer’s, Carpenter’s, Astrachan’s, 2 from Forrest & Hay, and the Present State Examination—CATEGO system. These operational definitions were generally shown to be internally reliable once psychiatrists were trained in their use. However, the various competing diagnostic systems were compared with respect to their reliability, concordance, and prediction of outcome8,9 and found to show wide disparity. For example, the systems varied by as much as 7-fold in their rates of diagnosing schizophrenia.10

These criteria which were primarily designed for research purposes were followed by the incorporation of similar operational rules for clinicians in the third edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-III)11 published in 1980. Like the Feighner criteria, the DSM-III definition of schizophrenia was narrow, requiring 6 months of illness before the diagnosis could be made.

In the Camberwell Register study conducted by Castle and colleagues,12 the authors examined the proportion of patients with a first episode of nonaffective psychosis who met different criteria. Nearly two-thirds of the 486 cases met the Research Diagnostic Criteria for either “broad” or “narrow” schizophrenia; this is not surprising given that this is the most liberal system, with no age-at-onset stipulation and only a 2-week illness duration requirement. However, only 32.6% of 486 cases fulfilled the criteria for schizophrenia in DSM-III and 32.3% for definite schizophrenia by the Feighner criteria, remarkably similar proportions which reflect the fact that the DSM-III criteria were much influenced by the St Louis school from which the Feighner criteria had emerged. Both the Feighner and DSM-III criteria had a high degree of predictive specificity, with one study showing no change in diagnosis over time using these criteria and an average of 6.5 years of follow-up.13

The Continuing Problem of Validity

With training, especially in the use of standardized interviews, DSM-III, like the other main competing system, produced acceptable interrater reliability. However, reliability does not necessarily mean validity and attempts to study validity as opposed to reliability were limited. Robins and Guze14 suggested 5 criteria to establish the validity of psychiatric diagnoses and illustrated their applicability to schizophrenia, namely, clinical description, laboratory studies, delimitation from other disorders, follow-up studies, and family studies. Kendler15 developed this approach by distinguishing between antecedent, concurrent, and predictive validators. However, although the intention in devising DSM-III was to use “research evidence relevant to various kinds of diagnostic validity”11 including “the largest reliability study ever done,”16 the committee chairman Robert Spitzer acknowledged that “the subjective judgment of the members of the task force … played a crucial role in the development of DSM-III, and differences of opinion could only rarely be resolved by appeal to objective data.”17

In 1994, DSM-IV was published.1 It shifted the emphasis on which psychotic symptoms were required for a diagnosis of schizophrenia, in that patients without either delusions or hallucinations could receive the diagnosis. In these cases, however, other characteristic psychotic symptoms were required, namely, gross disorganization of speech and/or behavior. The diagnostic importance of Schneiderian symptoms was also reemphasized, as hallucinations can satisfy a criterion if they involve one or more voices engaging in running commentary or ongoing conversation, and delusions can count if they are bizarre.18

However, to date, the DSM review process has not used external validators such as quantitative biological measurements or psychological testing to assist in the evaluation of diagnostic criteria or to judge whether changes are improving clinical validity. Furthermore, it did not prove better than the other systems, and ultimately it was the power and influence of the American Psychiatric Association rather than any innate scientific superiority of DSM-IV that determined that it became most widely accepted throughout the world.

An alternative to choosing between these definitions was to adopt a polydiagnostic approach, where several sets of criteria were applied to the same patients.19,20 One tool was the Operation Criteria Checklist for psychotic illness.21 This approach uses a suite of computer programs to generate diagnoses according to 13 different classification systems. It has been a useful adjunct to research methodology in light of the lack of a clear definition of the boundaries of schizophrenia and the wide variety of presentations. However, it is clearly impractical in everyday clinical practice.

Searching for Subtypes

Another alternative to establishing clear-cut and definable borders of schizophrenia was to suggest that it comprised several discrete subtypes and to use external criteria to try and validate these. The 1980s saw a number of attempts to account for diagnostic heterogeneity by probing for subtypes of schizophrenia, for example, positive, negative, and mixed schizophrenia22; familial and sporadic schizophrenia23; deficit and nondeficit schizophrenia24; and subtypes with some similarity to traditional hebephrenic and paranoid forms ("H" and "P" subtypes).25 Murray and colleagues26 later sought to
discriminate developmental from adult onset forms. Support for their hypothesis came from latent class analyses, but there remained the problem of intermediate forms. Furthermore, genetic and environmental risk factors were seen to operate across diagnostic categories.

**DSM-V: A Parochial System for Use in Certain Parts of North America or an International System?**

The reader will have noticed that the above discussion has been largely confined to proposals and papers emanating from Western countries, particularly the United States. The nosological paradigms developed to categorize different types of psychotic symptoms are embedded in specific professional cultures, but unfortunately, nosological discussions have rarely involved psychiatrists working in non-Western countries. This omission would be of little relevance to those preparing the DSM-V if it was merely to be used in the United States. However, the power of the American Psychiatric Association and American Psychiatry in general has resulted in the DSM-IV becoming the de facto system adopted by researchers throughout large parts of the world, indeed in preference to the International Classification of Diseases, 10th Revision. Clearly, if DSM-V seeks to be an international system, then it must address issues outside those of the USA.

**Research from Non-Western Countries**

Sadly, much of the research on psychotic conditions from developing countries—where the vast majority of individuals with psychotic conditions live—is unknown or dismissed as methodologically flawed by nosologists from developed countries. The substantial differences in the onset, course, and treatment response of psychotic symptoms between developed and less developed countries identified in the international pilot study on schizophrenia have had little effect on the dominant theories of psychosis which have all been developed in Western countries and based on data from developed countries. Furthermore, studies that identify acute remitting psychosis in developing countries have been largely disregarded by western nosologists. It is often assumed that methodological problems produce the “aberrant” findings, and so no attempt is made to identify other, more complex, explanations.

**Issues of Culture.** Thus, little attention has been paid to the fact that experience and understanding of psychotic symptoms are embedded in a network of local meanings that vary from nation to nation, within different subcultural groups in a single nation, and over time (as communities undergo sociocultural changes). Culture influences an individual’s perception of the world, the content of their thoughts, and therefore the form and quality of psychotic symptoms. It helps to determine the interpretation of symptoms and their subsequent social impact and guides both help seeking and the response to treatment. At a group level, culture can be considered important not only in defining and creating specific sources of stress and distress but also in providing specific modes of coping with distress and the social responses to distress and disability.

A good example of subcultural differences in the attitudes and help-seeking behavior of patients with schizophrenia and their families comes from China where there is a significant difference between patients from urban and rural areas. In rural areas, mental illness is often associated with malevolent spirits, and therefore, many families seek help from witch doctors. One study found that 73.9% (N = 286 of 387) of rural psychiatry outpatients admitted to previously consulting shamans, whereas only 4.9% (N = 21 of 426) of schizophrenia patients from an urban area in Beijing had done so.

A separate study suggested that while families of rural patients had a tendency to blame the illness on “external” factors such as spiritual forces, family members in urban areas were more likely to employ “internal” causal explanations. These included blaming the illness on pressure of studies, failure in love, or inability to adapt to a new competitive environment; less commonly used explanatory models involved physiological imbalances and psychological problems, such as personality quirks, excessive introversion, or nervousness. There was also a higher perceived effect of stigma in urban areas. Urban patients with a young age of illness onset are less likely to receive government-sponsored employment and to find a spouse, and therefore, they are considered socially inferior.

**Issues Concerning Ethnicity**

An influential study carried out by the World Health Organization was interpreted by its authors and others to suggest that the incidence of schizophrenia was unvarying. However, subsequent studies have demonstrated international, intranational, and cross-cultural differences in rates of psychotic illness. Furthermore, differences in the rates of schizophrenia have also been demonstrated for minority ethnic groups within a country. Thus, increased rates have been reported for the diagnosis of schizophrenia in migrant groups in Demark, France, Sweden, The Netherlands, and the United Kingdom. A recent meta-analysis of published studies by Cantor-Graae and Selten has demonstrated that different types of migrants have different risks of schizophrenia (table 1).

**The Curious Example of African Caribbeans in the United Kingdom.** The group that has been most intensively
The evidence is that there is a significant impact of living or being born in the United Kingdom, which puts those African Caribbeans already at genetic risk of developing schizophrenia at an even greater risk. Genetic vulnerability and the social/environmental context appear to be acting together in this cultural group to markedly increase rates.

Are the higher rates of psychosis in the African Caribbean UK population due to real increased rates of schizophrenia or are they due to misdiagnosis? In one study, a Jamaican psychiatrist was asked to make diagnoses on African Caribbean inpatients at a London teaching hospital. While the UK doctors diagnosed schizophrenia in 52% of patients and the Jamaican psychiatrist diagnosed schizophrenia in 55% of patients, the 2 only agreed on the diagnosis of schizophrenia in 52% of patients and the Jamaican psychiatrist diagnosed another psychosis in 55% of patients. The results were no different whether psychotic disorders with unique treatment pathways.

The difficulty in categorizing psychiatric illness is further underlined by differences in the course of schizophrenia between the African Caribbean community and native whites in the United Kingdom. African Caribbeans are approximately 40% less likely to suffer from a continuous illness than British whites and it is suggested that they are less likely to have a history of obstetric complications or neurological illness premorbidly. It has been hypothesized that the good symptomatic prognosis reflects increased rates of illness in less neurologically and genetically vulnerable people who have had relatively normal early development but have been exposed to social stressors that have promoted psychosis. One possible contributing factor is racial discrimination. Studies show that the darker the skin color, the more racism an individual is subject to regardless of mental illness.

One longitudinal study has demonstrated that those who experience discrimination are at an increased risk of developing delusional ideation. The lesson of these studies is that there may be a different balance of causes of psychosis, a different spectrum of symptoms, and a different outcome of psychosis in different populations.

### Findings from Recent Biological Studies

#### Pharmacology

Evidence that schizophrenia and bipolar disorder are not as dissimilar as the neo-Kraepelinian view suggests comes from studies showing that antipsychotics are effective in both conditions, thus implicating dopamine dysregulation as a key common mechanism in their etiology. For years, the responsiveness of bipolar disorder to lithium and other mood stabilizers was taken as a feature classically distinguishing it from schizophrenia. Recently, however, significant reduction in the severity of symptoms was observed in patients with an acute exacerbation of schizophrenia in whom divalproex was added to olanzapine or risperidone treatment. This builds upon earlier work by Brockington which showed that lithium and chlorpromazine were equally effective in schizoaffective patients and detracts from a notion that there are distinct psychotic disorders with unique treatment pathways.

#### Genetics

Schizophrenia and bipolar disorder occur together in the same families more frequently than chance. Furthermore, in a twin study using blinded diagnostic assessments and relaxing the normal hierarchical approach whereby schizophrenia trumps all other diagnoses, Cardno et al showed that if one member of a monozygotic twin pair has schizophrenia, there is about an 8% chance of the co-twin being diagnosed with schizoaffective disorder and an 8% chance of mania being diagnosed instead. Furthermore, as discussed elsewhere in this volume, recent molecular genetic studies, although as yet preliminary, suggest overlap between risk genes for schizophrenia and bipolar disorder.

#### Neuroimaging

Brain morphometry studies have shown that schizophrenia is associated with distributed gray matter deficits particularly in the frontotemporal neocortex, medial temporal lobe, insula, thalamus, and cerebellum, whereas patients with bipolar disorder have no significant areas of gray matter abnormality. However, both disorders show anatomically coincident white matter abnormalities in regions normally occupied by major longitudinal and interhemispheric tracts.
A Developmental Perspective

Thus, pharmacological, genetic, and neuroimaging studies suggest both similarities and differences between schizophrenia and bipolar disorder. Some understanding of the basis of these comes from adopting a life course perspective on the illnesses. Numerous studies have shown that preschizophrenic children are characterized by impairments in cognitive and neuromotor development. This was demonstrated very clearly in the Dunedin study which was also the first to demonstrate that these are not a feature of those who later develop bipolar disorder.56

Confirmation that bipolar patients do not have general neurocognitive impairment is provided by the Israeli Draft Board Registry study,57 which showed that 68 individuals hospitalized with bipolar disorder did not differ from their healthy matched counterparts on any test of intellectual, language, or behavioral functioning conducted routinely when they were adolescents. A more recent cohort study using national registers to follow all Swedish children who completed compulsory education showed that no students with excellent school performance developed schizophrenia or schizoaffective disorder. By contrast, achieving outstanding grades in certain school subjects was a significant predictor of later bipolar disorder.58

Further evidence that schizophrenia and bipolar disorders are at least partially distinct in etiology comes from studying complications of pregnancy and delivery. Obstetric events have been described as being more frequent in schizophrenia.59,60 Perinatal hypoxia arising from birth complications is particularly known to affect growth of the amygdala and hippocampus, which are often reported to be smaller in schizophrenia and not in bipolar disorder.61 There is no substantive evidence that obstetric complications increase the risk of bipolar disorder.62 Moreover, fetal growth indicators such as birth weight, birth length, and gestational age have also not been identified as risk factors for bipolar disorder.63

The similarities and differences between schizophrenia and bipolar disorder begin to suggest a model (figure 1) in which given a shared background of genetic predisposition to psychosis, additional specific genetic or early environmental insults interact to impair neurodevelopment, leaving individuals vulnerable to schizophrenia. By contrast, in bipolar disorder, developmental impairment is absent but syndrome-specific genes and environmental interactions may render individuals susceptible to social adversity.

A Dimensional Perspective

Traditionally, first-rank symptoms are given particular emphasis for making a diagnosis of schizophrenia rather than bipolar disorder. However, although Cardno and colleagues64 showed that a syndrome characterized by the presence of one or more first-rank symptoms has considerable heritability (71%, 95% confidence interval 57–82, compatible with a genetic contribution to variance in liability), it remains somewhat lower than that for schizophrenia as defined by established classifications, including DSM criteria.

An alternative to considering syndrome-based approaches to psychopathology is to use identified groups of correlated symptoms (symptom dimensions) in patient populations which comprise a range of diagnostic groups (shown schematically in figure 2). Different research teams have extracted usually 4 or 5 different factors or dimensions (eg, depressive, manic, positive, negative, and disorganization symptoms), and broadly these have been remarkably consistent between studies of different patient cohorts.

Recently, it has been shown that using such symptom dimensions explains more about disease characteristics (such as premorbid impairment, the existence of stressors before disease onset, poor remissions or no recovery between episodes and exacerbations, response to neuroleptics, and deterioration) than diagnoses alone and thus adds substantial information to diagnostic categories.66

Psychosis as a Dimension Reaching Into the General Population

Various groups have in recent years pointed out that minor psychotic symptoms occur in the general population and that psychosis is best conceived as a dimension like hypertension rather than a distinct category. (Refer to the review of Allardyce, van Os, and Gaebel70 for further discussion of dimensional representations of psychotic illness.) Further evidence also comes from studies of those at ultra high risk of developing psychosis.

There is ample evidence that psychosis is “brewing” long before its manifestation as a diagnosable illness71
and that identifiable signs and symptoms preceding the development of frank psychotic symptoms are evident.\textsuperscript{72} DSM-IV criteria for schizophrenia include this “prodromal phase” as a construct, but it describes a retrospective concept because it cannot be defined until there is an established psychotic illness. DSM-III\textsuperscript{11} identified 9 symptoms considered to be “prodromal” for schizophrenia and included them as diagnostic contributors. However, in a study by the Melbourne group based on retrospective conceptualization, these 9 symptoms were found to have specificities between 0.58 and 0.88 and positive predictive values between 0.36 and 0.48 but were not pathognomonic of schizophrenic psychosis.\textsuperscript{73}

Indeed, in one study, Yung and colleagues\textsuperscript{74} reported that for those ultra high-risk individuals who subsequently developed psychosis, diagnoses ranged from schizophrenia, through schizoaffective disorder, brief psychotic disorder, bipolar disorder to major depression. Using current “ultra high-risk” criteria, it appears as if early signs and symptoms are predictive of conversion to a spectrum of psychotic disorders but not of the exact nature of the psychosis that will develop.

It seems that the final diagnosis of a psychotic illness is merely the endpoint of a risk pathway which in itself is a slippery slope but not inevitable trajectory into psychosis (figure 3); this view is very compatible with the dimensional view of psychosis already discussed. In many cases, the pathway includes the development of prespsychotic symptoms, the development of frank but infrequent psychotic symptoms, the development of persistent psychotic symptoms, and finally social impairment due to these psychotic symptoms. Moving up or down the pathway depends on a balance between propsychotic factors such as individual biological vulnerability, the use of cannabis, and the social environment and antipsychotic factors such as individual resilience.

A Scheme Incorporating Developmental and Dimensional Ratings Offers a Possible Way Forward

There is great dissatisfaction with the DSM-IV concept of schizophrenia within North America, considerably more in Europe, and psychiatrists from the developing world regard it as largely ignoring the issues of 3 quarters of the globe. Difficulties in diagnosing mental illness among ethnic minority groups highlight the need for a universal classification system that can be effectively applied. However, the difference in rates of psychotic illness between countries and among different ethnic groups within a country also suggest that viewing culture and ethnicity as confounding variables in the conceptualization of mental illness is misguided. Rather, culture and ethnicity ought to be seen as fundamental elements driving its expression and interpretation.

By considering psychotic disorders from a life course perspective, including genetic factors, neurodevelopmental distinctions, symptomatology, structural neuroimaging, treatment strategies, and groups at ultra high risk of psychosis, we can see that a scheme which takes into consideration both developmental and dimensional characteristics as discussed above appears a possible way forward. For example, those at ultra high risk of psychosis would be rated at points on dimensions compatible with the extent and severity of their psychotic symptoms and affective symptoms. Whether or not they showed evidence of developmental impairment would help to predict the clinical picture of a full-blown psychosis if and when it developed. Again, as applied to African Caribbeans with psychosis in the United Kingdom,
such a model would suggest that this population is more vulnerable to a largely nondevelopmental illness in which social etiological factors are particularly important and which may present with a mixture of schizophrenic and manic symptoms.

However, whether diagnoses are based on symptom dimensions or diagnostic categories, the instruments for rating symptoms have typically been developed by selecting a subset of useful items from a large preliminary pool of items based on the results of a series of studies involving subjects in Western countries. If the entire process was repeated in a non-Western country, it would almost inevitably result in a very different instrument with different items and a different factor structure. For example, studies in China on symptom scales in schizophrenia have clearly demonstrated that translated and back-translated instruments can often achieve satisfactory test-retest reliability, but substantial revision is needed in order to achieve internal consistency and validity.

Another problem seen in the use of western diagnostic instruments in developing countries is the assumption that a single probe is sufficient to elicit a particular symptom; this is particularly problematic in fully structured diagnostic instruments that do not allow the interviewer to revise the question based on the educational and cultural background of the respondent. This single-probe method may work in developed countries where the experience and expression of psychological symptoms has been “homogenized” by frequent media exposure and other social forces; but for example in China, the huge sociocultural differences between urban and rural residents make it necessary to employ multiple probes to capture the different methods of experiencing and describing specific psychological symptoms.

Thus, if the DSM-V system of classifying psychosis is to be relevant to patients in the developing world, then instruments aimed at either making diagnoses or rating symptoms have to be subject to much more sophisticated field studies in non-Western countries than hitherto.

Proposal of a Hybrid System

It is clear that the categories of psychosis as used currently in DSM-IV are not valid in a strictly scientific sense. Their replacement by a developmental and dimensional approach as outlined above has much to recommend it for DSM-V. However, the current system does have some utility in terms of the information about etiology, course of illness, outcome, and treatment response that the different diagnoses convey. Abandoning it would be a very dramatic shift, and although we believe it would be an advance, some information of benefit to patients and clinicians would be lost.

We consider that at present the best option is to implement a hybrid of a categorical-dimensional approach in DSM-V. This would introduce the benefit of increased explanatory power of clinical characteristics, without completely dismissing the traditional paradigm of the Kraepelien dichotomy. Similarly, including a rating of developmental impairment would aid understanding of the longitudinal course of illness evolution, rather than considering a diagnosis as a cross-sectional perspective based only on the current clinical picture. Anything more radical is likely to be premature, with the expectation of further advances in genetic, neurobiological, environmental, and psychosocial research in the coming decade.

In parallel with research in individual disciplines, what is needed is a concerted multicenter effort to look back at existing epidemiologically based first-onset psychosis cohorts to investigate how external summary variables, including measures of cognition, social variables, and need for care, as well as symptom dimensions, familial liability scores, and basic structural magnetic resonance imaging data may sharpen the discriminative potential of the DSM classification of psychotic disorders. This should include cohort data from both developing as well as developed countries.

From our exploration of cultural issues, we suggest that standardized qualitative and quantitative methods need to be developed that can be employed in a wide range of different communities to conduct culturally sensitive assessments of psychotic symptoms. Only then will it be possible for the nosologist to attempt to identify universal “gold standard” criteria (preferably with unique biological and psychosocial markers) for a discrete set of psychotic diagnoses.

References
