Deconstructing Psychosis Conference February 2006: The Validity of Schizophrenia and Alternative Approaches to the Classification of Psychosis

Judith Allardyce, Wolfgang Gaebel2, Jurgen Zielasek2, and Jim van Os1

1Department of Psychiatry and Psychotherapy, Heinrich-Heine-University, Rhineland State Clinics, Düsseldorf, Germany

The DSM V planning process is currently underway and it has once again ignited the debate about the validity of the schizophrenia diagnosis. In this paper, we review the psychometric literature examining the evidence for discontinuity between schizophrenia and normality and the distinction between schizophrenia and other psychotic disorders. We conclude by proposing potential alternative approaches to refining the classification of psychosis.

Key words: psychosis/schizophrenia/classification/diagnosis/DSM V dimensions

Introduction

Worldwide, the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) definition of schizophrenia is the most influential in clinical practice and research. Its clear criterion-based definition facilitates diagnostic agreement (reliability) and communication among practitioners, including comparable statistical reporting of incidence and prevalence rates. It has high clinical utility, providing nontrivial information about course, outcome, and likely treatment response. However, does this make schizophrenia a valid diagnostic construct?

Clinical usefulness is embedded in the established criteria for nosological validation. A diagnosis is considered useful if its antecedent, biological, social, prognostic, or treatment correlates provide substantial information not contained within the syndrome’s definition. If we accept this conflation of utility and validity DSM-IV schizophrenia is indeed a robust construct, a model for conceptualizing complex clinical experience, guiding clinical management and predicting outcome.

Clinical utility, however, does not provide information about the fundamental nature and structure of schizophrenia; it does not answer the basic taxonic question “are the correlations of observed clinical characteristics, corroboration of underlying latent phenotypic dimensions (continuous distributions), latent categories (composed of one or more class or subdisorder, each with its own phenotypic presentation) or a mix of the two?” That is, usefulness does not provide information on the construct validity of schizophrenia. If our definition of schizophrenia does not represent a “real” construct in nature, then it will not delineate the true pathology and causal mechanisms underlying psychosis; it will obfuscate etiology. The developers of DSM-IV carefully point out that there is no assumption that each category is a discrete entity. However, they provide an operational definition of schizophrenia presenting the disorder as a condition qualitatively different from health (discontinuity between normality and schizophrenia) and qualitatively different from the other diagnoses (discontinuity between schizophrenia and the related diagnostic categories described in the classification system). Below, we review the evidence for this and discuss alternative approaches to the classification of psychosis.

The distribution of Psychosis in the General Population

Mounting evidence suggests that, in fact, there are no discrete breaks (demarcations) in the distribution of manifest (positive) symptom indicators of psychosis; delusions and hallucinations seem to have a continuous distribution in the general population. Prevalence estimates, in nonclinical samples, range from 4% to 17.5% (with methodological differences likely to explain much of this variability) and results from a longitudinal study using the British National Psychiatric Morbidity Survey data found that 4.4% of the general population reported incident symptoms at 18-month follow-up. These rates are not a reflection of unidentified cases “hidden” in the community because only a very small proportion of those reporting positive psychotic symptoms fulfilled diagnostic criteria for DSM nonaffective psychosis. How should we interpret this skewed continuum of positive psychotic symptoms? It may be an artifact, caused by measurement error; the use of lay interview or self-report methods may lower symptom recognition.

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thresholds, so studies are measuring psychosis-like experiences, not necessarily related to the clinical features of a true latent category or disease entity. However, even if there is measurement variance between the symptoms elicited in the general population and those from clinical samples, this may be informative, given the fact that psychosis-like symptoms can be conceived as indicators of psychosis proneness, “clinical psychosis” emerging (with higher than expected probability) from the pool of those with psychotic-like features.19,25–27

The skewed continuum may be indicative of a latent continuous pathology in the general population. This is consistent with the prevailing view that schizophrenia has a multifactorial etiology where many different genes, which are neither necessary or sufficient causes, and of small effect, interact with each other and with environmental risk factors to cause the disorder, different combinations of risk factors resulting in a gradation of exposure and associated range of presentations from normal through to the clinical disorder. Published work supports this postulated continuity in the risk factor profiles for community-reported symptoms and schizophrenia, though much of the evidence comes from cross-sectional studies where the direction of the associations cannot be determined for exposures that vary over the life course. One study has suggested that there may be some differences in risk factor profiles for psychotic symptoms and clinical psychosis,24 though this may in part be a consequence of using current urban residence as a proxy for urban birth and upbringing. If this finding is replicated, it would suggest discontinuity of risk factor profiles, though at a different point (threshold) on the indicator continuum than that suggested by the DSM-IV definition of schizophrenia.

These findings throw into doubt the assumption that schizophrenia exists as a discrete disease entity (categorical latent variable). The requisite population-based studies, using appropriate structural statistical analyses, eg, finite mixture modeling (and its derivates)28,29 or coherent cut kinetic methods30 have not been carried out, so it is still possible that a dichotomous latent construct could underlie the skewed distribution of psychosis indicators.10,31

The above approach uses delusions and hallucinations as indicators for the latent (continuous or categorical) construct schizophrenia. It remains possible that they are nothing more than epiphenomena or nonspecific surface symptoms, not core to the pathological process or perhaps even end-stage manifestations of schizophrenia.32 If this is the case, then positive psychotic symptoms may not provide adequate coverage of the latent construct whether it exists as a category or dimension in nature.

Schizophrenia: A Disorder Distinct from Other Psychosis?
The symptoms used to characterize schizophrenia do not define a specific syndrome. Rather, the concept allows a number of different combinations so that many permutations of the defining symptoms are possible (ie, it is a polythetic definition). These symptoms are also found commonly in the other categories of psychosis described in DSM-IV.33 Recent studies using psychopathological dimensions (correlations of symptoms determined by factor analysis) suggest that the diagnostic entities are similar with regard to the key symptom dimensions of psychosis.4,34–36 There is, however, variation in the dimensional profiles of different diagnostic categories in that individuals with a diagnosis of schizophrenia score higher in the positive, negative, and disorganized factors, while patients with affective diagnoses score higher in the manic and depressive dimensions and lower in the negative and positive dimensions.4,37 This seems to suggest a quantitative variation in symptom dimension scores across current diagnostic categories rather than qualitative differences. The factor solutions across studies have been broadly consistent demonstrating a 5-factor solution for psychosis—manic, depression, disorganized, positive, and negative (though there may be conflation of the disorganized and negative dimensions in first-onset samples).38 Reproducibility of this structure strengthens the findings. The true latent structure of psychopathology is still to be clarified, eg, latent class analyses (LCAs) demonstrate similar indicator profiles to those determined by exploratory factor analysis (EFA),39,40 confusing our understanding at the latent level. However, the overlapping co-occurrence of dimensions may be indicative of underlying shared risk factors, which are quantitatively rather than qualitatively distinct and continuously expressed. The ambiguous schizoaffective category may simply be the result of trying to demarcate, where in reality no latent discontinuity exists. Reasonable doubt exists about the true latent structure of the psychosis spectrum; therefore, the true appearance of psychosis in nature has yet to be determined.

Alternative Approaches to the Classification of Psychosis
Refinement of the Diagnostic Category (subtyping)
The clinical heterogeneity of DSM-IV schizophrenia could be reduced by refinement of the current definition, narrowing the concept, to describe more homogenous symptom clusters or subgroups.41,42 One putative categorical subtype is the “deficit syndrome,” characterized by enduring primary negative symptoms.43 Association studies support the clinical usefulness of this subgroup44–50 but tell us little about its construct validity. Does it truly exist in nature as a discrete disease entity (as its definition assumes) or are its observed associations with external validators the result of comparing high scoring individuals with those scoring low on a latent (negative) dimension? If negative symptoms are associated with other important variables in the clinical, neurocognitive, social, or biological domain, any comparison
of individuals high vs those low in negative symptoms will yield significant group differences regardless of whether or not the true latent structure of negative symptoms is purely dimensional. A recently published study, using coherent cut kinetics, suggests that there may be a latent level discontinuity in negative symptoms within (chronic) schizophrenia, with an estimated base rate of 28%–36%. The author’s were unable to compare this empirically defined construct with that of deficit syndrome because they had not rated deficit symptoms in their sample. Further support for a possible discrete negative subcategory of schizophrenia comes from a study which used a surface data reduction method (principal components analysis [PCA]) to identify dimensions of psychopathology and found the negative factor scores were bimodally distributed in people with a diagnosis of schizophrenia.4 If the PCA factor does represent a latent dimensional construct (which is not necessarily the case), then this suggests a quantitative discontinuity in the negative dimension.

An important limitation of this approach, however, is the use of chronic clinical samples because this can lead to artificial truncation of the symptom severity distribution, which can distort the results by violating the conditional independence assumption needed to obtain unbiased estimates.50,52,53

**Dimensional Representations**

Another approach that has been used extensively to reduce the clinical heterogeneity seen in schizophrenia is by statistically identifying psychopathological dimensions (groups of symptoms which occur together more often than would be expected by chance alone) using factor analyses. Individuals can then be defined by how high or low they score on the different dimensions, which may coexist. This methodology assumes that the underlying latent structure of psychopathology is continuous. A 3-factor solution has consistently been found in schizophrenia, and when affective symptoms are included, a further 2 factors are identified, namely depressive and mania/excitement.54 Expanding this method to include more broadly defined functional psychosis have generally extracted similar 4- or 5-factor solutions.38,55–58 Differential associations are consistently found across the symptom dimensions with clinically relevant variables.4,37,59-61 Analyses comparing dimensional representations with the traditional diagnostic categories show the dimensions to be more useful at predicting clinical course and treatment needs, though the difference in the discriminative power may be rather small.4,59,62 Thus, dimensions seem to add to the information contained within the diagnostic systems, providing assessments that are more detailed and likely to be important particularly in clinical research.

Both these alternative methods for classification (subtypes and dimensions) use latent variable modeling to tap into the underlying structure of psychopathology. However, the approach to date has important limitations. Taxonic analyses have rarely been carried out, prior to the LCA or EFA. Therefore, the decision about which statistical method to use has not been empirically driven but rather reflects the researcher’s epistemological stance. If a latent class (taxon) is identified, external analyses (association studies) can be carried out on this subsample of individuals to determine secondary thresholds (subgroups). Failure to restrict these analyses to the taxonic group will introduce unnecessary imprecision into the search for secondary thresholds. On the other hand, if no taxon is identified, it is appropriate to use factor analyses or multidimensional scaling to generate symptom scores, which can be used in external (association) analyses to define diagnostic thresholds. It is important to remember that a latent class can be extracted as a strong factor in EFA (30). Kessler has proposed a 3-tiered approach for the use of structural analyses in the development of psychiatric classification systems.52

**Search for More Proximal Indicators of Psychosis**

The current definition of schizophrenia and the alternative approaches discussed in this article depend heavily on symptoms and signs that are probably somewhat distal to the underlying pathoetiology. Integration of defining characteristics, more proximal to the pathological process underlying schizophrenia, is likely at some point in the future (reviewed in accompanying articles in this issue). Potentially informative, alternative indicators of psychopathology are the development of standardized and validated functional clinical tests for psychological dysfunction (dysfunctional modules).63 A modular concept of psychopathology is grounded in experimental psychological theory, and depends on a model where psychological behavior and brain structure constitute a modular system, made up of identifiable microsubsystems of elementary psychological functions, with corresponding neuronal circuits, distributed networks,64 or processing streams. A series or hierarchy of dysfunctional modules would then provide a detailed and individual characterization of an individual patient.

**Conclusion/Recommendations**

Two main diagnostic issues arise. First, it is essential to know how the psychosis phenotype or phenotypes exist in nature, in order to study its causes and outcomes. Second, a decision needs to be made about how to derive a useful diagnostic construct from the natural phenotype or phenotypes, so that patients can be usefully identified and treated.

In the short term, there is considerable need for descriptive and latent variable approaches to determine how psychosis is distributed in the general population.
Identification of naturally occurring taxons, and/or continuous dimensional representations of psychopathology, and their associated course and outcome over time may be clinically very useful.

In the longer term, these descriptive approaches will no doubt be complemented by studies of putative etiological or pathophysiological indicators. However, until this time, the aim of any revision of our classification system should be to optimize clinical utility. The emerging evidence seems to demonstrate that models using both categorical and dimensional representations of psychosis are better discriminators of course and outcome than either model independently. Currently, the most useful approach to classification seems to be the complementary use of categorical and dimensional representations of psychosis.

References


