

# Dimensions and the psychosis phenotype

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## Abstract

*In this paper, we discuss the conceptual background for including a dimensional component to the DSM V diagnoses for psychoses. We review the evidence for a continuous distribution of psychosis like symptoms in the general population and summarise the research validating the clinical usefulness of psychopathological dimensions. We conclude that diagnostic models using both categorical and dimensional representations of psychosis have better predictive validity than either model independently. Dimensions do not appear to be diagnosis specific so a flexible scoring of dimensions across all psychotic and major affective disorders may be potentially more informative than a system where categorical diagnoses are kept artificially dimension-specific. Copyright © 2007 John Wiley & Sons, Ltd.*

**Key words:** Psychosis, schizophrenia, bipolar affective disorder, dimensions, psychosis continuum, psychosis phenotype.

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The current Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) classification of psychosis stems directly from the systematic clinical observations of Kraepelin (1919), Bleuler (1911) and Schneider (1959) who worked in the large asylums of Western Europe during the late nineteenth and early twentieth century. These institutions provided care for people with severe and debilitating conditions. There are at least two potentially important limitations to a classification system derived from such a selective case sample. First, your clinical experience would be of severe cases in need of treatment, you would understandably conceptualize psychosis as a discrete disease entity, as a categorical construct, distinct from normality. This, however, may not reflect the true distribution of psychosis at the population level.

Second, the observed pattern of psychopathological co-occurrence may actually reflect symptoms, which are independent risk factors for hospital admission becoming conditionally dependent in the institutional setting, a phenomena known as Berkson's fallacy (bias). A community study has shown that positive and nega-

tive symptoms are both independently associated with need for care (Maric et al., 2004). Such additive effects could inflate the positive/negative co-occurrence in hospital settings, indicating that the current conceptualization of schizophrenia as a unitary entity with high co-occurrence of positive and negative psychopathological domains may in part be the result of Berkson's bias.

Similar findings apply to the bipolar disorder construct. A general population study has demonstrated independent associations of manic and depressive symptoms, with need for care; while symptom co-occurrence was 17% in individuals known to services it was only 7% in those not in the secondary health care system. These independent effects may well inflate depression/mania co-occurrence in institutional settings (Regeer et al., in press).

There is no doubt that the work of Kraepelin, Bleuler and Schneider respectively (and the classification systems which evolved from their insights), has greatly facilitated the acquisition of the knowledge we now have about psychosis. However, the walls of the asylum

confined their observations, perhaps obscuring the true nature of the psychosis phenotype.

### Distribution of psychosis in the general population

The clinical definitions of psychosis may represent only a minor, possibly biased sample of the total psychosis phenotype present in the general population. This is consistent with the prevailing view that psychosis has a multi-factorial aetiology (similar to that seen in other chronic disorders such as diabetes and cardiovascular disease) where many different genes, which are neither necessary or sufficient causes, and of small effect, interact with each other and with environmental risk factors (Jones and Cannon, 1998). It can be shown that such different combinations of risk factors must result in a gradation of exposure and associated range of different expressions from normal through to clinical psychosis (continuum hypothesis). Mounting support for the continuum hypothesis comes from studies examining (1) the distribution of psychotic symptoms and psychotic proneness in the general population; (2) the pattern of genetic and non-genetic risk factor profiles in non-clinical and clinical samples; (3) the transition from sub-clinical to clinical states over time (up to 25% in the largest prospective study to date (Poulton et al., 2000)).

The distribution of the positive symptoms of psychosis, delusions and hallucinations, seem to have a continuous distribution in the general population (Eaton et al., 1991; Janssen et al., 2003; Johns et al., 2004; Kendler et al., 1996; King et al., 2005; Olfson et al., 2002; Peters et al., 1999; Poulton et al., 2000; Tien, 1991; van Os et al., 2000a; van Os et al., 2001; Verdoux et al., 1998; Wiles et al., 2006; Spauwen et al., 2003). Prevalence estimates, in non-clinical samples, range from 4% (Eaton et al., 1991) to 17.5% (van Os et al., 2000a) (with methodological differences likely to explain much of this variability). High rates do not appear to be secondary to measurement error due to self-report interview techniques, as high rates are also reported using non self-report interviews by clinicians (Poulton et al., 2000; Spauwen et al., 2003). These rates also are not a reflection of unidentified cases 'hidden' in the community, as only a very small proportion of those reporting positive psychotic symptoms fulfilled diagnostic criteria for DSM non-affective psychosis (Kendler et al., 1996; van Os et al., 2000a). That the psychosis phenotype is much more prevalent than previously thought is also supported by recent work

showing that the lifetime prevalence of psychotic disorder, when multiple sources are taken into account, exceeds 3%, much higher than the traditional 0.6% (Perala et al., 2007). Studies of schizotypy (a personality trait characterized by a proneness to psychotic-like experiences) suggest that it is a quantitative rather than a qualitative trait, on a continuum from normality, through eccentricity, different combinations of schizotypal characteristics, to florid psychosis. Factor analyses of schizotypy extract three or possibly four dimensions: aberrant perceptions and beliefs, introvert/anhedonia and conceptual disorganization (a factor solution some consider to be similar to that found in schizophrenia). This work suggests that psychosis proneness is a multi-dimensional continuous construct (Gruzelić, 1996; Mata et al., 2003; Vollema and van den Bosch, 1995).

Mood disturbance similarly appears to have a continuous distribution in the general population. Sub-threshold depression and (hypo)mania, defined as the experience of distinct periods of depressive or (hypo)manic symptoms, which do not fulfill the DSM-III-R/IV diagnostic criteria appear to be common (Angst and Gamma, 2002; Cuijpers et al., 2004) with prevalence rates of up to 13% for depression, and 9% for hypomania (Angst and Merikangas, 1997; Angst et al., 2003).

Evidence from longitudinal and cross-sectional studies of risk factors in general support a continuity of risk profiles for subclinical and clinical psychosis (Chapman et al., 1994; Kwapil et al., 1997; Peters et al., 1999; van Os et al., 2000a; van Os et al., 2001; Verdoux et al., 1998). However, one study has demonstrated some differences, which will require further evaluation. Partly, these differences may be due to study design; for example, the study measured the effect of current urban residence on psychotic symptoms, in elderly individuals who are likely to have moved many times and are at very low risk of developing incident psychotic symptoms, rather than studying urban birth/upbringing in young individuals who are most at risk for psychotic symptoms (Wiles et al., 2006).

Finally, longitudinal studies suggest that clinical psychosis emerges, from the pool of those with psychotic-like features, with a much higher than expected frequency (Bebbington and Nayani, 1995; Chapman et al., 1994; Hanssen et al., 2005; Poulton et al., 2000). Non-clinical manic symptoms also appear to represent risk indicators for future clinical manic episodes (Regeer et al., 2006). Interestingly, the probability of developing

incident bipolar disorder is substantially higher (approximately 7%) in individuals with both subclinical manic and psychotic symptoms (Kaymaz et al., 2006).

These studies suggest, that both manic and psychosis phenotypes occur as part of a continuum from normality through to full-blown clinical disorders, that is, they are fundamentally dimensional in nature.

Superimposing categorical diagnoses on latent continuous constructs results in loss of information, but this practice may yield useful short-hand approximations to facilitate communication among clinicians. Potential problems arise, however, if the categories are arbitrary or generated from samples with selection bias (e.g. from the severe end of the spectrum or institutional settings), where they potentially 'misrepresent' the underlying patho-aetiology. This is likely to impede our further understanding of the causes and correlates of psychosis. It may in part explain the current lack of replicable findings in the genetic and biological study of schizophrenia and bipolar disorder.

It is important to keep in mind that although a continuum of psychosis and bipolarity may exist, the diagnosis of need for care and the decision to treat always will remain dichotomous. Need for care results from the interaction between continuous phenotype and the person in terms of, for example, coping, social support, and the level of comorbid developmental impairment

### **Clinical psychosis: discrete category or psychopathological dimensions**

Categories of psychoses defined in DSM-IV reflect historical notions of severe mental illness observed in institutionalized clinical settings. As discussed earlier, such settings may inflate the co-occurrence of symptoms, obscuring their true latent nature and generating spurious categories. The different psychotic diagnoses overlap in their pre-morbid risk factors, clinical presentations, management needs and outcomes (Murray et al., 2004). This lack of discrimination casts doubt as to how clinically useful the categorical classification systems used today are (McGorry et al., 1998; Toomey et al., 1997), and has resulted in a search for alternative representations of psychoses. One approach is to identify psychopathological dimensions (groups of symptoms which occur together more often than would be expected by chance alone) using exploratory factor analyses (EFA). Individuals can then be defined by how high or low they score on the different dimensions,

which may co-exist. The initial work in this area examined the factor structure of the diagnostic category of schizophrenia and found evidence for a three-factor solution (Bilder et al., 1985; Liddle, 1992, 1987; Peralta et al., 1992), extracting positive, negative and disorganized factors. The disorganization factor is the most unstable and least replicable of the three dimensions. However, a two-factor solution does not adequately represent the symptom correlations (Peralta et al., 1994) and the three factor solution may in fact represent higher order factors of many more first order dimensions (Peralta and Cuesta, 1999). A five-factor solution with additional manic and depressive dimensions is found when measures of affective symptoms are included (Lindenmayer et al., 2004). When samples are expanded to include the full spectrum of psychoses, broadly similar five-factors solutions are found, (Dikeos et al., 2006; Kitamura et al., 1995; Lindenmayer et al., 2004; McGorry et al., 1998; McIntosh et al., 2001; Murray et al., 2005; Ratakonda et al., 1998; Serretti et al., 2001; Serretti and Olgiati, 2004), though there may be conflation of the disorganized and negative dimensions especially in first onset samples (McGorry et al., 1998). It seems that the dimensions generated from established cases of psychosis provide reasonably replicable, stable solutions in a variety of settings, diagnostic groups and patient samples; however the factor structure may be less stable around the time of presentation (Drake et al., 2003).

### *The clinical validity of dimensional representations of psychosis*

Nosological constructs such as psychopathological dimensions should be useful, that is, provide non-trivial information about course, outcome and likely treatment response (Kendell, 1989). A number of studies have examined the association of psychopathological dimensions with various clinically significant characteristics. The most consistent finding is a strong association of the negative dimension with indicators of poor (chronic deteriorating) course (Dikeos et al., 2006; Hollis, 2000; Marengo et al., 2000; van Os et al., 1996; Wickham et al., 2001). The disorganization factor also predicts poor outcome but this is a weaker and less consistent finding. The associations of other dimensions are inconsistent and markedly attenuated after adjustment for diagnosis (Dikeos et al., 2006).

A more informative method of assessing the usefulness of the dimensional approach is to compare the rela-

tive contribution of the dimensional factor scores and diagnostic categories in predicting the variability of clinically significant characteristics. Such studies consistently show the dimensional representations to be more useful at predicting clinical course and treatment needs, though the difference in the discriminative power may be rather small (Dikeos et al., 2006; Peralta et al., 2002; Rosenman et al., 2003; van Os et al., 1996).

One study has shown that while factor scores add to the predictive power of the diagnostic categories, the diagnostic categories did not increase the predictive power of the dimensional scores. This seems to suggest that the current diagnoses may partition symptom dimensions appropriately. However, models using both categorical and dimensional representations have better discriminative validity, suggesting that the most powerful approach to classification is the complementary use of both categorical diagnoses and dimensional scores (Dikeos et al., 2006).

### Practical example

The following clinical example illustrates how concomitant categorical and dimensional assessment may facilitate patient-care. A 45-year-old man with a 20-year history of bipolar I disorder, presents with mild hypomanic symptoms; reduced need for sleep (2–3 hours less than usual per night), bright and cheerful affect, increased energy, and subjectively feels very productive at work. He has worked as an insurance agent manager of a large company for 10 years, where he is regarded as a conscientious, focused, calm, and task-oriented employee. At interview, he describes plans to reorganize the branch and carry this model throughout the company. This expansive mildly grandiosity does not meet criteria for delusional thinking, but may be on a continuum with delusional grandiose thought. Use of a dimensional measurement would alert the clinician to offer appropriate intervention to avert manic relapse which, if unmanaged, would escalate over a few days. His thought content would move to not only changing his branch, but also going to the head office to tell them how to run the company and telling them he should be CEO. This is one example for the mood case of mania. Similar examples could readily be drawn for patients diagnosed with schizophrenia, mania, or depression.

### Potential limitations of a dimensional approach

To date, with different studies suggesting different numbers of factors or variations in factor composition,

there is no definitive model for the symptom dimensions of psychosis, though the five-factor model comprising positive, negative, disorganized, manic and depression dimensions is increasingly being considered to have internal validity. Most exploratory factor analytical studies have used chronic or mixed stage samples, however; if there are psychopathological changes during the course of a disorder (Fenton and McGlashan, 1991; Eaton et al., 1995; Peralta and Cuesta, 2001), samples with different distributions of 'stage of disorder' will yield different symptom dimensions depending on the dominant stage studied. For example, there is no study in the current literature examining the predictive validity of symptom dimensions in first-episode cases of psychosis.

The current diagnostic categories facilitate diagnostic agreement (reliability) and communication among practitioners (Kendell and Jablensky, 2003) and it may be that the introduction of dimensional measures could threaten this. However, what is being proposed initially is a dimensional measure that will complement the categorical diagnosis, perhaps generated from rating scales known to have relatively high inter-rater agreement – for example, the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987). Symptom-rating scales are now used routinely in clinical settings to monitor treatment response and relapse and to assess remission. The introduction of a formal dimensional measure in the classification system would hopefully, coordinate and optimize this use.

It is important to decide over which diagnostic categories we measure any proposed psychotic dimensions. The revised classification system could be organized around the presence/absence of psychosis. However, it is quite possible that psychotic symptoms are not fundamental core features of the underlying diseases, but rather, non-specific, perhaps even end-stage manifestations of a number of different pathological processes (Goldman-Rakic, 1995). Crow (1990) has suggested that there exists an aetio-pathological continuum across schizophrenia, schizoaffective disorder, and affective illness, and a recent study of patients with psychotic and non-psychotic bipolar disorder and schizophrenia found a specific association between neurotrophin-4 core-at-risk haplotype and 'manic' forms of schizophrenia and 'bipolar' forms of schizophrenia supporting a biological continuum (Green et al., 2005). The literature suggests that substantial 'hidden bipolarity' would be found in patients with unipolar depression

if a mania dimension were additionally scored in the course of the diagnostic process (Benazzi and Akiskal, 2003; Cassano et al., 2004), and negative symptoms have been demonstrated in patients with bipolar disorder (van Os et al., 2000b). The flexible scoring of dimensions across all psychotic and major affective disorders potentially could be more informative than a system where categorical diagnoses are kept artificially dimension-specific.

### Conclusion/recommendations

It is essential that we understand how the psychosis phenotype or phenotypes exist in nature, in order to study their determinants and outcomes. Further elucidation is likely to come from studies using descriptive and latent variable methodologies to identify fundamental categorical subtypes and/or continuous dimensions of psychopathology. In the future, it is likely these descriptive approaches will be complemented by the inclusion of putative aetiological or pathophysiological indicators.

An ever-increasing number of published studies continue to examine dimensional approaches in schizophrenia and bipolar disorder. Dimensions are not diagnosis-specific, yet current categorical diagnoses require dimensional specificity. In the psychosis literature, affective and non-affective dimensions have been identified in people with psychosis, whereas in individuals with major mood syndromes, psychotic versus non-psychotic domains have been studied. A more productive approach may be to study dimensionality across all mood and psychotic syndromes.

The current evidence supports the complementary use of both categorical and dimensional representations of psychosis. Diagnostic models using both categorical diagnoses and dimensions have better predictive validity than either model independently, and flexible scoring of dimensions across all patients with psychotic and major affective disorders is likely to be especially informative.

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