

## Psychopathology factors in first-episode affective and non-affective psychotic disorders

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### Abstract

**Background:** Since the onset, prevalence, and course of specific psychopathological features rarely have been analyzed simultaneously from the start of dissimilar psychotic illnesses, we compared symptom-clusters in first-episode DSM-IV affective and non-affective psychotic disorders.

**Methods:** Subjects ( $N = 377$ ) from the McLean–Harvard First Episode Project hospitalized for first-lifetime primary psychotic illnesses were followed prospectively for 2 years to verify stable DSM-IV diagnoses. We ascertained initial symptoms from baseline SCID and clinical assessments, applying AMDP and Bonn psychopathology schemes systematically to describe a broad range of features. Final consensus diagnoses were based on intake and follow-up SCID assessments, family interviews, and medical records. Factor-analytic methods defined first-episode symptom-clusters (Factors), and multiple-regression modeling related identified factors to initial DSM-IV diagnoses and to later categories (*affective*, *non-affective*, or *schizoaffective* disorders).

**Results:** Psychopathological features were accommodated by four factors: **I** represented *mania with psychosis*; **II** a *mixed depressive-agitated* state; **III** an *excited-hallucinatory-delusional* state; **IV** a *disorganized-catatonic-autistic* state. Each factor was associated with characteristic prodromal symptoms. Factors I and III associated with DSM-IV mania, II with major depression or bipolar mixed-state, III negatively with delusional disorder, IV with major depression and negatively with mania. Factors I and II predicted later affective diagnoses; *absence* of Factor I features predicted non-affective diagnoses, and no Factor predicted later schizoaffective diagnoses.

**Conclusion:** The findings contribute to descriptive categorizations of psychopathology from onset of dissimilar psychotic illnesses. This approach was effective in identifying and subtyping affective psychotic disorders early in their clinical evolution, but non-affective and schizoaffective conditions appear to be more complex and unstable.

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### 1. Introduction

The psychopathological and nosological constructs of primary psychotic illnesses have undergone intense theoretical debate since the origins of clinical psychiatry (Baethge et al., 2003; Trede et al., 2005). Current taxonomies (WHO, 1992; APA, 2000) use a *categorical*-hierarchical scheme to

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diagnose and subtype psychotic disorders, conceptually based on the Kraepelinian dichotomy between schizophrenia-like psychotic versus major affective disorders with psychotic features (Trede et al., 2005). Alternative approaches include searching for pathognomonic features (Bleuler, 1950; Schneider, 1959) or attending to psychopathological dimensions (Crow, 1980; Liddle, 1987), with less concern about diagnostic categorization. However, such a *dimensional* approach has focused largely on defining schizophrenia, with less effort to distinguish *among* disorders with psychotic features. Lack of compelling support for either categorical or dimensional models has encouraged searching for links between etiology and phenomenology (Tsuang et al., 1990), or an emphasis on defining domains of psychopathology that might relate to particular pathophysiological or genetic disturbances (Buchanan and Carpenter, 1994; Flaum et al., 1995; Sabri et al., 1997; Crow, 1998; Serretti et al., 2000; Alfimova and Uvarova, 2002), as well as defining external validators, such as family history, demographic or historical features, longitudinal course, or treatment effects (Johnstone and Frith, 1996; Pavuluri et al., 2004).

Despite efforts to develop alternative methods of defining disorders, standard psychiatric diagnostic systems (WHO, 1992; APA, 2000) continue to conceive of primary non-affective and affective psychotic disorders as discrete syndromes based on distinct symptom structures, courses, and outcomes. For better or worse, in the continued absence of etiologic, pathophysiological, or genetic criteria, early 21st-century psychiatric nosology remains dependent on descriptive clinical criteria, despite considerable overlap of psychopathological features and common intermediate syndromal types recognized at least since Kraepelin (Pope and Lipinski, 1978; Trede et al., 2005). We propose that psychiatric nosology has remained insufficiently sensitive to the heterogeneity among individual and groups of psychotic disorder cases. This limitation and an overwhelmingly descriptive approach, probably have limited progress in both clinical and biological studies (McGorry et al., 1990; Cuesta and Peralta, 2001).

Comparing affective vs. non-affective psychotic syndromes, and studying the evolution of their psychopathological patterns from illness-onset are key elements of research on psychosis constructs (Arndt et al., 1995; McGorry et al., 1998; Cuesta et al., 2003). Modern multivariate statistical methods provide new approaches to identifying clinical typologies (Manton et al., 1994; Kendler et al., 1998) and developing dimensional models within syndromal categories (Van Os et al., 1996, 1999; Serretti et al., 1996; McGorry et al., 1998; Cuesta et al., 2003). At the very least, further progress in differentiating psychotic disorders requires simultaneous consideration of broad groups of patients with psychotic features, close investigation of individuals early in the evolution of their illnesses, and a longitudinal-ontogenic perspective based on long-term follow-up, with due regard to artifacts associated with long-term illness and disability, as well as effects

of treatment and institutionalization (McGorry et al., 1998; Tohen et al., 2003; Meagher et al., 2004).

In response to these requirements, we report on initial exploration of symptom structure in a large and clinically heterogeneous sample of first-episode psychotic patients, using modern factor-analytical techniques, exploring the longitudinal evolution of symptom patterns, and comparing initial symptom-clusters to secure DSM-IV diagnoses established over time.

## 2. Materials and methods

### 2.1. Subjects and diagnostic assessments

We studied 377 subjects from the McLean–Harvard First-Episode Project who presented in a first-lifetime episode of psychotic illness in 1989–1995 and gave written informed consent, following annually updated project review and approval by the McLean Hospital IRB, in accord with the latest version of the Declaration of Helsinki. Exclusion criteria were: (a) acute intoxication or withdrawal syndrome associated with drug or alcohol abuse, or any delirium; (b) previous psychiatric hospitalization, unless for detoxification; (c) presence of mental retardation (IQ <70) or other DSM-IV organic mental disorder; (d) index syndromal illness present >6 months or previous syndromal episode; or (e) prior total treatment with an antipsychotic  $\geq 4$  weeks or mood-stabilizer for >3 months.

Diagnoses were based on SCID-P assessments at baseline and at two years, followed by a best-estimate, investigator-consensus procedure based on all available information, and were updated to meet DSM-IV-TR criteria in 2000–2003, as reported previously (Tohen et al., 2000, 2003). At baseline, 138 subjects (36.6%) met DSM criteria for non-affective psychotic disorders (schizophrenia, delusional, schizophreniform or brief psychotic disorder, or psychosis not otherwise specified [NOS]). Another 239 (63.4%) met criteria for major affective disorders with psychotic features (bipolar-manic, bipolar-mixed, bipolar-NOS, or major depressive disorder), and none was considered schizoaffective. Outcome diagnoses are considered below.

### 2.2. Clinical assessments

To develop a comprehensive, systematic, and detailed inventory of specific psychopathological features, we used the widely employed 100-item *Manual for the Assessment and Documentation of Psychopathology* (AMDP) (Guy and Ban, 1982) and 66-item *Bonn Scale for Assessment of Basic Symptoms* (BSABS) (Gross et al., 1987). These broad schemes include affective, behavioral, cognitive, psychotic, sensory, and social dimensions of psychopathology. The AMDP system includes definitions and operationalized criteria for 100 symptoms and other clinical features derived from classic psychopathology studies, including Jaspers (1913), Bleuler (1950), Schneider (1959), and others, and

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