Phenomenology and diagnostic outcome of first-episode psychosis

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Background and objectives
The establishment of criteria for the definition of first-episode psychosis is complex. The literature on this topic is controversial in terms of the limits of duration of symptoms and the inclusion of prodromal symptoms, together with symptoms of the acute phase. Defining first-episode psychosis and determining the diagnostic outcome in the short term for early recognition and intervention might contribute significantly toward reducing later morbidity and chance of recovery. The aim of the current study is to examine the clinical presentation both at baseline and at short-term follow-up (2 years) with determination of the diagnostic outcome on the basis of systemic and structured instruments and frequent follow-up.

Methods
Ninety drug-naïve patients were recruited consecutively from among inpatients after the exclusion of patients with first-contact psychosis who had neurological or central nervous system problems, chronic medical conditions, a history of or current substance abuse or dependence and mental subnormality. Assessment at baseline and after 2 years by structured DSM-IV interviews (SCID), PANSS, HDRS, YMRS, and WAIS as well as WMS-III. Demographics and clinical characteristics were obtained, and a consensus diagnosis was made on the basis of structured instruments, medical records, collateral information, and face-to-face interviews.

Results
Patients with first-episode psychosis were divided into three diagnostic outcome groups: schizophrenia spectrum ($n=49$; 54.4%), bipolar psychosis ($n=21$; 23.3%), and depressive psychosis ($n=20$; 22.2%). Patients in the schizophrenia spectrum were predominantly men, single, and students with no educational differentiation and with no familial risk compared with patients with other two diagnoses. Younger age, early age of onset, long duration of untreated psychosis and short duration of untreated illness, and low rate of hospitalization, but with longer duration of stability and higher sensitivity for extrapyramidal side effects were reported more in the schizophrenia spectrum group than the affective spectrum group. Cognitive functions were better in bipolar and depressive psychosis both at baseline and at the short-term assessment (2 years later) compared with schizophrenia spectrum patients, who showed more improvement after 2 years of assessment on attention and executive function than effective ones. Higher severity of depression was recorded on depressive psychosis in both steps of assessment than that in patients with bipolar schizophrenia. The mean YMRS scores were higher in patients with bipolar psychoses, followed by schizophrenia patients than the depressive group. PANSS five-factor analysis showed that negative symptoms and cognitive disorganization were the highly significant differentiating aspect of the schizophrenia spectrum group than the affective spectrum patients.

Conclusion and recommendations
Overlap of symptoms and clinical presentation in patients of first-episode psychosis both at baseline and for short-term outcome is quite common. Interacting longitudinal and cross-sectional assessment may help to clarify this complexity of presentation at first-episode psychosis. Focus on the differentiation of primary and secondary symptoms in researches as well as biological findings is important to clarify this heterogeneity.

Keywords:
affective spectrum, first-episode psychosis, phenomenological symptom presentation, schizophrenia spectrum

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Introduction

Historically, the term 'psychosis' has had several definitions. In older diagnostic classifications, the definition of 'psychosis' was very broad, focusing on the severity of functional impairment, and a given mental disorder was termed 'psychotic' if it resulted in relevant interference with the individual's capacity to conform to the demands of daily life. In the current diagnostic classifications, the use of the term is basically restricted to the prominent presence of delusions and/or hallucinations and/or disorganized speech and/or disorganized behavior (including catatonia), with no insight into the nature of these symptoms, indicating a broad impairment in one's capacity to make critical judgments of reality (American Psychiatric Association, 2000).

The establishment of criteria for the definition of first-episode psychosis is even more complex. The literature on this topic is controversial with respect to the limits of the duration of symptoms and the inclusion of prodromal symptoms, together with the symptoms of the acute phase, for the definition of first-episode psychosis (Beiser *et al.*, 1993; Fennig *et al.*, 1994; Jackson *et al.*, 1994; Schwartz *et al.*, 2000).

The *Diagnostic and Statistical Manual of Mental Disorders*, 4th ed. (DSM · IV) and the International Classification of Diseases, 10th revision (ICD-10) systematize psychotic illnesses as distinct, complex, multifactorial categorical conditions defined by a broad range of symptom characteristics used to guide the differential diagnosis (World Health Organization, 1994; First *et al.*, 1996; American Psychiatric Association, 2000). Diagnostic differentiation is achieved using psychological, cognitive, and behavioral symptomatology, as well as information on the course of illness. Efforts to refine these diagnostic criteria are reflected in ongoing revisions of diagnostic manuals used worldwide. No unique or disorder-specific symptoms have been identified for psychotic disorders; thus, multidimensional criteria are used to make differential diagnoses in clinical practice (Peralta and Cuesta, 2005). Recent studies of the clinical characteristics of psychotic disorders have highlighted their common overlapping clinical features (Murray *et al.*, 2004; Dikeos *et al.*, 2006). For example, it is not uncommon for patients with schizophrenia to have symptoms of depression and for Schneiderian first-rank symptoms to be present in patients with psychotic affective disorders (World Health Organization, 1973; Hafner *et al.*, 2005; Rosen *et al.*, 2011).

The examination of phenomenological similarities and differences in psychotic disorders at illness onset is important for at least two reasons. First, such studies carried out close to the onset of illness can potentially identify differentiating clinical features of these disorders independent of the effects of illness course and chronic medication treatments and, thus, provide evidence of the relatively unique and common manifestations of these disorders. Second, from a practical point of view, studies of the phenomenology of these disorders early in course of illness can guide differential diagnosis and treatment planning for first-episode patients when information on the course of illness is not yet available (Andreasen *et al.*, 1995; Sass and Parnas, 2003).

Schizophrenia and psychotic affective disorders have been classified both categorically and dimensionally. Emil Kraepelin played an important role in differentiating disorders now named bipolar disorder and schizophrenia, using information on both the symptoms and the course of illness (Kraepelin, 1971). He considered manic depression as an episodic illness with periods of considerable recovery of function and dementia praecox as a degenerative persistent condition leading to poor outcome and negative symptoms as primary characteristics. Of note, in later writings, Kraepelin came to view this diagnostic dichotomy as insufficient to explain the dimensional heterogeneity in the clinical presentation of these conditions (Kraepelin, 1992). It has even been argued that many of Kraepelin's patients who were considered to have dementia praecox may not fulfill the current diagnostic criteria for schizophrenia (Boyle, 1990).

Eugen Bleuler developed the concept of schizophrenia (Bleuler, 1950; Stotz-Ingenlath, 2000). Blueler's concept expanded the fundamental psychological characteristics of schizophrenia to include disorganization (i.e. the 'loss of association' in thought processes), recognition of affective features, and the existence of a continuum within schizophrenia (schizophrenia simplex to complex). His views generally had greater use of defining symptoms relative to the course of illness for a clinical diagnosis. Recently, models have been proposed to treat bipolar disorder and schizophrenia as ends of a continuum rather than as discrete diagnostic entities (Crow, 1991, 1995; Tsuang *et al.*, 2000) because of uncertainties on the boundaries of these conditions. This blurring of the boundaries of schizophrenia and affective psychoses is reflected in the consideration of variants such as schizoaffective disorder, and has led to the proposal that these psychotic disorders may result from similar or overlapping pathophysiological mechanisms (Andreasen, 2006; Van and Tamminga, 2007).

In the absence of specific biological markers, careful longitudinal follow-up remains a crucial method for determining the validity of psychiatric diagnoses Robins and Guze (1970) included the outcome and stability of diagnosis over time as two of the five criteria for establishing diagnostic validity. Kraepelin distinguished the poor outcome of dementia praecox from the more benign outcome and episodic course of manic-depressive psychosis. Evidence of diagnostic stability is also important for validation because it is likely to reflect a stable underlying psychopathological process (Fennig *et al.*, 1994). In adults, definitions of schizophrenia that include duration criteria (e.g. DSM-II, DS'M-III-R, DSM-IV, and Feighner criteria) have higher levels of diagnostic stability (Tsuang *et al.*, 1981; Mason *et al.*, 1997) and better predictive validity than definitions of schizophrenia on the basis of Schneiderian first-rank symptoms.

The early recognition and intervention offer a unique opportunity to implement measures to prevent occasional

impairments and complications that are inherent to chronic disorders. These measures include the definition of the most adequate drug treatment and the implementation of psychosocial interventions that might contribute significantly toward the reduction of later morbidity, thus leading to greater chances of recovery (Mc Gorry *et al.*, 2008).

The primary aim of this study was to examine the differences in clinical symptom presentation in a sample of consecutive patients presenting with their first psychotic episode to determine the extent of overlap and differentiation in psychopathological signs and symptoms and formulation of diagnostic outcomes after 2 years of prospective follow-up.

Patients and methods

Place and design

The current prospective study was carried out at the psychological Medicine Hospital, State of Kuwait. This is the only and official Psychiatric hospital (1200 beds) that provides psychiatric services at the tertiary level.

The research was approved by the research and ethics committee. All patients had to sign an informed consent either by themselves or their caregivers who live with them.

The current study had two parts:

(1) Baseline assessments: all patients with first-contact psychosis admitted from January 2008 to December 2009 were assessed by clinical and Psychometric scales.
(2) End of 2 years of follow-up: patients were assessed by all clinical and psychometric studies used at baseline. The study was completed at the end of December 2011.

Inclusion criteria

All patients included in this study were drug naïve, with first contact to the psychiatric facility, and were accompanied by a close family member who lived with them. Patients of both sexes were recruited if they were older than 18 years of age. Only Kuwaiti patients were included in order to avoid cultural impact and to be easy to reach during follow-up.

Exclusion criteria

Patients with any major medical illness or neurological disorder, seizure, mental subnormality, or a history of head trauma with loss of consciousness for more than 10 min as well as those with a history of or current substance abuse or dependence were all excluded from the study.

Process

At the end of the recruitment period, we had 176 patients with first-episode psychosis. Only 139 patients were Kuwaiti; 18 of them did not fulfill the inclusion criteria and 11 refused to participate in the study. We had 110 patients who completed the baseline study. By the end of 2 years, only 90 patients were available and completed the study. Patients were compared with 23 healthy control participants.

Consensus diagnoses were made by members from the clinical and research team using the structured clinical interview of DSM-IV (First *et al.*, 1996), and all available collateral information from families and/or previous caregivers, medical records, and information provided from the clinical and research team. This information generally included not only initial symptoms but information obtained by direct and ancillary information over the course of 6–8 weeks of initial treatment. Repeated clinical assessments were performed every 6 months or at the time of each rehospitalization.

Of the 90 eligible patients, 49 patients (54.4%) were diagnosed with schizophrenia spectrum disorders (schizophrenia, $n = 44$), schizoaffective disorder ($n = 5$); 21 patients with psychotic bipolar disorder (23.3%); and 20 patients with unipolar depression with psychosis.

Measures

Positive and Negative Syndrome Scale (Kay et al., 1987)

Positive and Negative Syndrome Scale (PANSS) items are scored along a continuum of severity between 1 (asymptomatic) and 7 (extreme symptom severity).

Analyses were carried out both on the total scale and subscale (positive, negative, and general psychopathology) scores as well as using data reduction strategies on the basis of previous empirical studies of symptom domains assessed by PANSS:

(1) Positive symptoms (scores of delusions, grandiosity, suspiciousness/persecution, unusual thought content items).
(2) Negative symptoms (scores of blunted affect, emotional withdrawal, poor rapport, passive/apathetic social withdrawal, lack of spontaneity and flow of conversation items, and finally active social avoidance).
(3) Cognitive disorganization (conceptual disorganization difficulty in abstract thinking, mannerisms and posturing, disorientation, and poor attention).
(4) Excitement (excitement, hostility, tension, and poor impulse control).
(5) Depression (somatic concern, anxiety guilt feelings, depression, and preoccupation).

The above-mentioned PANSS items were pooled in this way on the basis of previous factor analytic findings (Lindenmayer *et al.*, 1994; Lehoux *et al.*, 2009).

PANSS items were also pooled into three-dimensional clusters on the basis of previous cluster analysis research (Farmer *et al.*, 1983; Morrison *et al.*, 1990; Dollfus *et al.*, 1996) as follows:

(1) Anergia (blunted affect, emotional withdrawal, motor retardation, and disorientation).
(2) Thought disturbance (conceptual disorganization, hallucinating behavior, grandiosity, and unusual thought content).
(3) Paranoia (suspiciousness of persecution, hostility, and uncooperativeness).

Hamilton Depression Rating Scale (Hamilton, 1960, 1967)
The original version had 17 items [Hamilton Depression Rating Scale (HDRS 17)] related to symptoms of depression experienced over the past week. A score of 0–7 is generally considered to be within the normal range (or in clinical remission), 8–13 is considered to indicate mild severity of depression, 19–22 moderate severity, and more than 23 as very severe degree of depression.

Young Mania Rating Scale (Young et al., 1978)

(1) Young Mania Rating Scale (YMRS) is an 11-item clinician-rated scale designed to assess the severity of manic symptoms over the previous 48 h both for baseline assessment and for follow-up of treatment response.
(2) Four of the YMRS items were scored on 0–8 scale, with the remaining five items being rated on a 0–4 scale. A score of up to 12 indicates remission of symptoms.

Cognitive tests
A standardized cognitive battery was completed by all participants once they were clinically stable; it was tested and scored by one of our trained researchers who was not involved in the treatment of the patients either at the baseline assessment or at the end of the 2-year follow-up. Cognitive ability was examined by dividing various neuropsychological tests into six cognitive domains as suggested by NIMH–measurement and treatment research to improve cognition in schizophrenia (Measurement and Treatment Research to Improve Cognition in Schizophrenia, 2003; Nuechterlein *et al.*, 2004).

The following domains were derived:

Working memory: from spatial span subtests of the Wechsler Memory Scale, 3rd ed. (WMS-III) (Wechsler, 1997) and the Digit span subtests of Wechsler Adult Intelligence Scale, 3rd ed. (WAIS-III) (Wechsler, 1997).

(1) Verbal learning and memory – from the logical memory subtest of WMS-III.
(2) Visual learning and memory – from the visual reproduction subtests of WMS-III.
(3) Speed and processing: from the trail-making test A (completion time (Reitan, 1992) and the digit symbol subtest of WAIS-III.
(4) Reasoning and problem solving: from the trail-making B and the block design subtest of WAIS-III.
(5) Attention: from spatial span and the Digit span forward subtest of WAIS-III.

Intellectual ability: using Wechsler Adult Intelligence Scale
Verbal and performance subtest; intelligence quotient (IQ) was measured both at baseline and at follow-up (2 years).

Statistical methodology
Data were collected and coded, and then entered into an IBM compatible computer using SPSS version 17 (SPSS Inc., Chicago, Illinois, USA) for windows. The data entered were checked for accuracy and then for normality using the Kolonogorov–Smirnov test.

Qualitative variables were expressed as numbers and percentages, whereas qualitative variables were expressed as measures (X) and SD.

The arithmetic means (X) were used as a measure of central tendency whereas the SD was used as a measure of dispersion.

The following statistical tests were used:

(1) Independent-samples t-test was used as a parametric test of significance for comparison between two sample means after performing Levene's test for equality variances.
(2) Independent-samples Mann–Whitney's U-test (or Z-test) was used as a nonparametric test of significance for comparison between two sample medians.
(3) The χ^2-test (or log likelihood ratio) was used as a nonparametric test of significance for comparison between the distribution of two qualitative variables.
(4) The Kruskal–Wallis test (χ^2-value) was used as a nonparametric test of significance for one-way comparison between more than two sample means when the one-way analysis of variance test was not appropriate.
(5) Spearman's rank correlation coefficient was used as a nonparametric measure of the mutual relationship between two non-normally distributed qualitative or ordinal variables.
(6) Multivariable logistic regression analysis for prediction of factors that may affect diagnostic outcome.
(7) A 5% level was chosen as a level of significance in all statistical significance tests used.

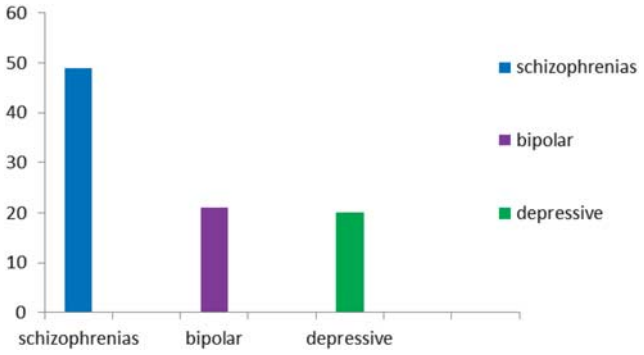
Results

(1) In the current research, we studied 90 patients with first-episode psychosis consecutively at baseline and at follow-up for 2 years. The consensus diagnosis had been made by members from the clinical and research team using a structured interview for DSM-IV, collateral information from families, and caregivers, and review of medical records at different points of the 2-year follow-up every 3–6 months and/or at rehospitalization.
(2) Forty-nine patients were diagnosed with the Schizophrenia spectrum, representing 54.4% of the total sample; 21 patients (23.3%) had bipolar psychoses and 20 patients (22.2%) had depressive psychoses (Table 1 and Fig. 1).
(3) Group comparisons of demographics showed a significant sex difference between the three groups. Patients with schizophrenia spectrum disorders were predominantly men ($P = 0.03$), single, and students ($P = 0.000$), but with no significant difference in the level of education in comparison with both bipolar and depressive patients (Table 1).
(4) Table 1 also shows that the schizophrenia group had a low familial history of psychosis compared with the bipolar and depressive groups ($P = 0.005$).

Table 1 Demographics and clinical characteristics of first-episode psychosis patients with different diagnostic outcomes

	N (%)			
	Schizophrenia spectrum (*n*=49)	Bipolar psychoses (*n*=21)	Depressive psychosis (*n*=20)	*P* value
Sex				
Male	39 (79.59)	12 (57.14)	10 (50.0)	0.03
Female	10 (20.41)	9 (42.86)	10 (50.0)	–
Marital status				
Married	7 (14.29)	5 (23.81)	8 (40.0)	–
Single	39 (79.59)	10 (47.62)	6 (30.0)	0.000
Divorced	3 (6.12)	6 (28.57)	6 (30.0)	–
Education				
Primary	6 (12.24)	5 (23.81)	2 (10.0)	–
Secondary	16 (32.65)	8 (38.10)	10 (50.0)	–
University	24 (48.98)	7 (33.33)	7 (35.0)	0.87
Postgraduate	3 (6.12)	1 (4.76)	1 (5.0)	–
Job				
Student	30 (61.22)	4 (19.05)	3 (15.0)	–
Professional	4 (8.16)	4 (19.05)	6 (30.0)	–
Manual work	11 (22.45)	6 (28.57)	5 (25.0)	0.00
Not working	4 (8.16)	7 (33.33)	6 (30.0)	–
Family history				
Negative	35 (71.43)	16 (76.19)	15 (75.0)	0.005
Positive	14 (28.57)	5 (23.81)	5 (25.0)	–
Types of antipsychotics				
Resperidone	13 (26.53)	3 (14.29)	0 (0)	–
Olanzapine	16 (32.65)	8 (38.10)	9 (45.0)	–
Quitiapine	13 (26.53)	7 (33.33)	11 (55.0)	0.000
Haloperidol	6 (12.24)	2 (9.52)	0 (0)	–
Sulpride	1 (2.04)	1 (4.76)	0 (0)	–

Figure 1



Diagnostic outcome in first episode psychosis.

(5) Atypical antipsychotics (resperidone, olanzapine, and quitinpine) were highly significantly prescribed for schizophrenia than the affective groups (Table 1) ($P = 0.000$).
(6) Table 2 shows that the mean antipsychotic dosage (chlorpromazine equivalent) was significantly higher in patients with depressive and bipolar psychoses than in those with schizophrenia.
(7) Patients with the schizophrenia spectrum had the longest duration for stability with drug treatment, whereas patients with depression psychoses had higher rehospitalization rates ($P = 0.000$) (Table 2) than the other two groups.
(8) Patients with schizophrenia were significantly younger and had early onset of illness by 3.5 years than bipolar and depressive patients ($P = 0.000$).

Phenomenology of first-episode psychosis

Cognitive function

At baseline assessment: group comparison of different cognitive functions showed that the baseline mean scores for working memory, verbal memory, visual memory, attention, and executive function (speed and processing, reasoning, and problem solving) and also baseline intellectual abilities in patients with depressive psychoses were higher than those in bipolar and schizophrenia patients. This was clear in spatial back ($P = 0.03$), logic memory immediate ($P = 0.05$), visual reproduction immediate and delayed, ($P = 0.02$, 0.001), spatial span forward ($P = 0.04$), Digit symbol ($P = 0.007$), and Trial making A ($P = 0.01$) cognitive tests (Table 3 and Fig. 1).

At the end of 2 years: patients with depressive and bipolar diagnosis had higher mean scores for all cognitive functions than schizophrenia patients (Table 4 and Fig. 2)

This means that patients with first-episode psychosis diagnosed with schizophrenia spectrum had poor cognitive function in comparison with patients with affective psychosis (bipolar and depressive groups).

As shown in Table 5, the rate of improvement in cognitive function – indicated by percent change in cognitive function at the end of the 2 years compared with baseline assessment – was higher for affective psychoses patients (bipolar and depressive) than the schizophrenia spectrum group. This improvement was obvious in working, verbal, and visual memory; however, the rate of improvement was higher in schizophrenia patients for attention and executive function (speed and processing, reasoning, and problem solving) than in bipolar and depressive patients. This was true also for percent change in verbal performance and total WAIS scores.

Affective symptoms

Depression (Table 6 and Fig. 3): patients with depressive psychosis showed a moderate degree of depression indicated by the HDRS mean score (19.40 ± 3.79), with higher ratings on depressed mood, sleep disturbance, guilt feeling, somatization, motor retardation, agitation, and hypochondriasis and suicide.

In contrast, the mean score of HDRS for schizophrenia and bipolar patients was comparable (9.67 ± 3.5 and 9.38 ± 2.4), indicating a mild degree of depression. The higher score was for middle insomnia for bipolar patients, whereas guilt feeling, middle and late insomnia were more in schizophrenia group.

At the end point of the study (2 years), the rate of improvement was highly significant in all symptoms for all groups. Schizophrenia and bipolar patients showed normal range of depression (HDRS-scores), whereas patients with depressive psychosis had a mild degree of depression (HDRS score = 10.25 ± 3.37).

Mania (Table 7 and Fig. 4): using YMRS, patients with bipolar psychosis showed higher scores indicating a severe form of mania (YMRS score = 46.38 ± 5.7) at baseline assessment. Irritability, thought content disturbances,

Table 2 Characteristics of first-episode psychosis patients with different diagnostic outcomes

	Schizophrenia spectrum ($n=49$)		Bipolar psychoses ($n=21$)		Depressive psychosis ($n=20$)		
	Mean	SD	Mean	SD	Mean	SD	*P* value
Current age (years)	21.84	2.88	25.38	4.41	30.60	8.56	0.000
Age at onset (years)	20.55	2.19	23.38	2.09	25.95	4.20	0.000
Rehospitalization	1.47	1.24	1.19	1.63	4.45	5.02	0.000
Chlorpromazine equivalent drug dosage (mg)	251.84	175.16	276.67	73.37	288.50	46.34	0.000
Duration of treatment stability (days)	12.00	3.70	8.81	2.34	7.85	1.84	0.000

Table 3 Cognitive functions for different diagnostic patient groups of first-episode psychosis at baseline

	Schizophrenia spectrum		Bipolar psychosis		Depressive psychosis		
	Mean	SD	Mean	SD	Mean	SD	*P* value
Working memory							
Spatial back	5.41	1.04	6.02	0.82	6.16	0.05	0.03
Digit back	5.86	0.67	6.11	0.81	5.91	0.89	0.41
Verbal memory							
Logic memory immediate (LMI)	32.66	2.10	34.1	1.7	36.6	0.75	0.05
Logic memory delayed (LMD)	20.57	1.91	22.9	2.2	25.7	0.89	0.08
Logic memory recall (LMR)	23.17	0.96	23.6	0.58	25.6	0.63	0.65
Visual memory							
Visual reproduction immediate recall (VRI)	86.61	11.7	88.5	2.5	92.33	2.21	0.02
Visual reproduction delayed recall (VRD)	70.67	6.5	72.8	3.7	87.42	3.00	0.001
Visual reproduction recognition (VRR)	43.91	0.66	44.1	0.29	45.31	0.54	0.63
Attention							
Spatial span forward	6.77	0.43	8.33	0.54	8.4	0.38	0.04
Digit span forward	9.19	0.46	9.91	0.63	10.3	0.27	0.12
Speed and processing							
Digit symbol	64.77	0.55	70.63	1.07	74.9	0.96	0.007
Trail making – A	37.75	4.51	32.81	3.1	28.1	1.4	0.01
Reasoning and problem solving							
Trail making – B	85.11	12.71	79.81	3.71	81.00	0.86	0.61
Block design	41.31	1.55	46.83	0.70	47.4	0.65	0.08
WAIS IQ							
Verbal	56.95	3.43	62.7	2.2	61.8	1.9	0.75
Performance	45.12	3.16	51.3	2.7	51.7	2.9	0.32
Total score	101.81	7.51	114.1	4.3	113.6	3.7	0.14

The higher the scores, the better the performance of the patient, except for the Trail-making test (measured in seconds).
IQ, intelligence quotient; WAIS, Wechsler Adult Intelligence Scale.

speech disturbances, (rate and amount), aggression, sleep disturbances, increased motor activity, and impaired insight had higher mean scores.

Patients with schizophrenia showed less manic manifestation on YMRS (mean = 19.6 ± 8.07), with higher scores on thought content disturbances, disruptive aggressive behavior, irritability, increased motor activity, and impaired insight. In contrast, patients with depressive psychosis had the lowest mean score of YMRS (mean = 6.5 ± 3.1).

By the end of the study, the symptoms of mania showed a highly significant improvement in all groups of patients but with a marked response in bipolar patients, in whom the mean total score of YMRS decreased from 46.38 ± 5.7 to 10.62 ± 2.9.

Psychosis

Tables 8 and 9 show PANSS five factor and cluster scores as well as positive, negative, and general psychopathology subscales scores, comparing schizophrenia spectrum, bipolar psychosis, and depressive psychosis patient groups at baseline assessment and after 2 years (Figs 5 and 6).

Patients with schizophrenia had significantly greater negative symptoms, cognitive disorientation, and thought disturbances as well as anergia than bipolar and depressive psychosis patients.

Psychotic bipolar patients showed significant higher scores in positive symptoms, excitement, and paranoia than schizophrenia and depressive groups. However, depression was the only factor that was higher in the depressive psychosis group than the other two groups.

Interestingly, the rate of improvement of impaired cognitive disorganization and negative symptoms in schizophrenia patients was significantly lower compared with the improvement observed in both depressed and bipolar patients.

The rate of improvement in other factors, for example positive symptoms, depression, excitement, papanoia, anergia, and thought disturbances was comparable in all patient groups (Table 9).

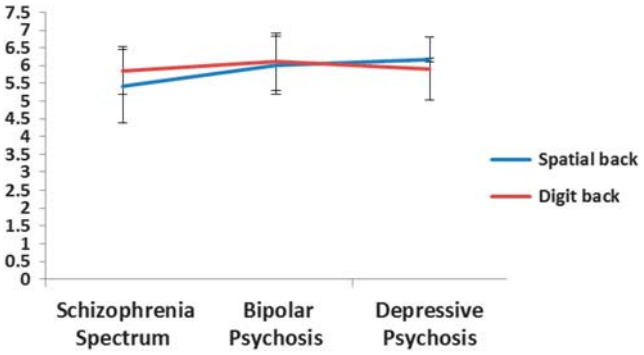
The severity of PANSS factor scores and item clusters highlights symptom overlap across diagnostic groups in the acute phase of a first episode of psychosis. Negative

Table 4 Cognitive function for schizophrenia spectrum, bipolar psychosis, and depressive psychosis of patients with first-episode psychosis at the end of 2 years of follow-up

	Schizophrenia spectrum		Bipolar psychosis		Depressive psychosis		
	Mean	SD	Mean	SD	Mean	SD	*P* value
Working memory							
Spatial back	5.7	1.3	6.2	0.66	6.4	0.27	0.064
Digit back	6.1	1.07	6.5	0.84	6.5	0.26	0.41
Verbal memory							
Logic memory immediate	33.3	2.7	35.6	3.3	37.2	0.94	0.23
Logic memory delayed	21.5	3.1	24.6	2.5	26.3	0.92	0.05
Logic memory recall	23.3	1.6	24.3	0.41	26.2	0.67	0.05
Visual memory							
Visual reproduction immediate recall	89.5	3.6	90.8	2.2	93.01	2.1	0.66
Visual reproduction delayed recall	72.08	7.1	76.3	7.3	88.2	2.8	0.001
Visual reproduction recognition	44.1	1.06	44.5	0.46	45.7	0.57	0.21
Attention							
Spatial span forward	7.3	0.87	8.2	0.25	7.8	0.49	0.02
Digit span forward	9.7	0.69	10.2	0.36	10.8	0.26	0.25
Speed and processing							
Digit symbol	66.5	2.7	72.3	3.7	75.7	0.96	0.00
Trail making – A	35.5	5.1	31.9	3.5	26.6	1.3	0.01
Reasoning and problem solving							
Trail making – B	80.4	9.4	74.5	8.3	79.2	3.4	0.04
Block design	42.6	1.7	46.9	1.4	47.9	0.76	0.03
WAIS (IQ)							
Verbal	57.9	4.5	62.8	4.1	62.3	1.9	0.66
Performance	54.8	4.2	52.7	3.3	52.2	3.1	0.42
Total score	104.0	8.2	116.4	4.3	114.6	3.7	0.32

The higher the scores, the better the performance of the patient, except for the Trail-making test (measured in seconds).
IQ, intelligence quotient; WAIS, Wechsler Adult Intelligence Scale.

Figure 2



Comparison of working memory for different diagnostic patient groups of first-episode psychosis at baseline assessment.

symptoms and cognitive disorientation were the only persistent symptoms at follow-up.

Predictors of diagnosis

By logistic regression analysis using many variables, aiming to predict the diagnosis at baseline assessment or even at the end of the 2-year follow-up, unfortunately, current age, sex, age of onset of duration if untreated illness, duration of untreated psychosis, scores of HDRS, YMRS, PANSS, or even baseline intellectual abilities (WAIS-IQ scores) were not predictors for diagnosis in any of the groups.

Discussion

The clinical importance of differentiating psychotic disorders as early as possible can guide different treatment plans and help reduce morbidity. This was the main concern of the researchers during the planning of this study.

Patients in the schizophrenia spectrum group were higher in number (54.4%) than patients with affective psychosis bipolar (23.3%) and depressive (22.3%). The large number of patients being diagnosed with schizophrenia over the course of illness has been reported in various studies (Abd El-Azim, 2007; Subramaniam *et al.*, 2007; Haahr *et al.*, 2008).

Sociodemographics and clinical characteristics

The controversy and inconsistency in the demographics and clinical characteristics of the sample make it difficult to differentiate between affective and noneffective psychosis.

The most powerful factors differentiating affective psychosis from schizophrenia spectrum psychosis in the current study were sex, duration of untreated psychosis age of onset, and familial risk.

A significant number of schizophrenia patients were men; this has been replicated in many studies (Lewine *et al.*, 1984; Castle *et al.*, 1993; Aleman *et al.*, 2007).

Other studies have reported that the incidence and prevalence of schizophrenia is the same in men and women (Wyatt *et al.*, 1988, Perala *et al.*, 2007; McGrath *et al.*, 2008).

Younger age and early age at onset were clear in schizophrenia spectrum patients than in patients with bipolar or depressive psychosis. This was in agreement with the results of Bromet *et al.* (2005) and Haahr *et al.* (2008).

Table 5 Percent change in different cognitive functions for patients with first-episode psychosis at the end of 2 years of follow-up

	Mean ± SD			
	Schizophrenia spectrum	Bipolar psychosis	Depressive psychosis	*P* value
Working memory				
Spatial back	5.18 ± 10.7	10.68 ± 13.32	4.93 ± 3.96	0.076
Digit back	5.72 ± 11.14	8.39 ± 11.35	15.1 ± 42.11	0.32
Verbal memory				
Logic memory immediate	1.92 ± 4.80	4.33 ± 9.17	1.64 ± 1.10	0.26
Logic memory delayed	4.63 ± 9.39	7.70 ± 8.10	2.33 ± 1.25	0.08
Logic memory recognition	0.077 ± 4.38	3.05 ± 3.98	2.35 ± 1.06	0.005
Visual memory				
Visual reproduction immediate recall	1.23 ± 1.33	2.55 ± 2.90	0.70 ± 0.28	0.72
Visual reproduction delayed recall	2.41 ± 9.43	4.65 ± 6.25	0.90 ± 0.42	0.25
Visual recognition	0.24 ± 2.35	1.03 ± 1.54	1.02 ± 0.73	0.000
Attention				
Spatial span forward	8.54 ± 13.06	− 1.13 ± 6.97	6.03 ± 3.89	0.001
Digit span forward	6.37 ± 6.44	3.07 ± 6.17	4.33 ± 2.01	0.035
Speed and processing				
Digit symbol	2.74 ± 4.17	2.42 ± 5.02	1.04 ± 0.50	0.56
Trail making – A	− 5.75 ± 6.60	− 2.22 ± 11.41	− 5.41 ± 2.66	0.11
Reasoning and problem solving				
Block design	3.13 ± 3.90	0.17 ± 2.07	1.13 ± 0.76	0.000
Trail making – B	− 8.80 ± 11.41	− 6.59 ± 9.84	− 2.23 ± 3.8	0.83
IQ				
Verbal	1.73 ± 4.86	0.21 ± 7.36	0.90 ± 0.98	0.63
Performance	1.40 ± 5.45	2.75 ± 4.98	0.85 ± 0.97	0.46
Total	2.31 ± 6.05	2.10 ± 3.40	0.89 ± 0.69	0.53

IQ, intelligence quotient.

Table 6 Hamilton Depression Rating Scale in different diagnoses of first-episode psychosis at baseline assessment and at the end of 2 years of follow-up

	Schizophrenia spectrum (*n* = 49)			Bipolar psychoses (*n* = 21)			Depressive psychoses (*n* = 20)		
	Baseline Mean ± SD	End of 2 years Mean ± SD	*P* value	Baseline Mean ± SD	End of 2 years Mean ± SD	*P* value	Baseline Mean ± SD	End of 2 years Mean ± SD	*P* value
1. Depressed mood	0.41 ± 0.50	0.27 ± 0.45	0.14	0.00 ± 0.00	0.14 ± 0.36	0.08	2.35 ± 0.81	1.20 ± 0.52	0.000
2. Work and activity	0.08 ± 0.28	0.00 ± 0.00	0.04	0.10 ± 0.30	0.00 ± 0.00	0.16	0.95 ± 1.32	0.45 ± 0.69	0.008
3. Genital symptoms	0.20 ± 0.71	0.00 ± 0.00	0.04	0.00 ± 0.00	0.00 ± 0.00	–	0.65 ± 0.81	0.25 ± 0.44	0.008
4. Somatic symptoms	0.04 ± 0.20	0.00 ± 0.00	0.15	0.00 ± 0.00	0.14 ± 0.36	0.08	0.45 ± 0.51	0.20 ± 0.41	0.02
5. Loss of weight	0.08 ± 0.28	0.00 ± 0.00	0.04	0.19 ± 0.40	0.00 ± 0.00	0.04	0.10 ± 0.31	0.05 ± 0.22	0.33
6. Insomnia (early)	0.06 ± 0.24	0.00 ± 0.00	0.083	0.10 ± 0.44	0.10 ± 0.30	1.00	1.05 ± 0.94	1.00 ± 0.79	0.66
7. Insomnia (middle)	1.92 ± 1.06	1.16 ± 0.55	0.00	2.86 ± 1.01	1.05 ± 0.38	0.00	2.00 ± 1.12	1.25 ± 0.64	0.002
8. Insomnia (late)	1.86 ± 1.02	1.02 ± 0.80	0.00	0.57 ± 0.75	0.19 ± 0.40	0.008	2.5 ± 0.95	1.30 ± 0.98	0.000
9. Somatic symptoms	0.98 ± 1.23	0.081 ± 0.28	0.00	1.24 ± 0.83	0.24 ± 0.44	0.000	1.20 ± 1.67	0.30 ± 0.66	0.02
10. Feelings of guilt	1.82 ± 1.58	0.43 ± 0.74	0.00	1.48 ± 1.12	0.90 ± 1.00	0.000	2.20 ± 1.54	0.70 ± 0.92	0.001
11. Suicide	0.69 ± 0.77	0.06 ± 0.24	0.00	0.19 ± 0.40	0.00 ± 0.00	0.04	1.00 ± 0.86	0.95 ± 0.76	0.85
12. Anxiety – psychic	0.06 ± 0.24	0.02 ± 0.14	0.32	0.05 ± 0.22	0.00 ± 0.00	0.32	0.15 ± 0.37	0.35 ± 0.49	0.10
13. Anxiety somatic	0.22 ± 0.42	0.04 ± 0.20	0.005	0.38 ± 0.50	0.00 ± 0.00	0.002	0.60 ± 0.60	0.10 ± 0.31	0.00
14. Hypochondriasis	0.00 ± 0.00	0.41 ± 0.50	0.00	0.00 ± 0.00	0.00 ± 0.00	–	1.30 ± 0.47	0.90 ± 0.45	0.002
15. Insight	0.00 ± 0.00	0.00 ± 0.00	0.00	0.10 ± 0.44	0.05 ± 0.22	0.32	0.20 ± 0.89	0.20 ± 0.52	1.000
16. Motor retardation	1.27 ± 0.57	0.82 ± 0.39	0.00	1.57 ± 0.60	0.76 ± 0.44	0.000	1.15 ± 0.95	0.15 ± 0.37	0.000
17. Agitation	0.00 ± 0.00	0.00 ± 0.00	0.00	0.62 ± 0.50	0.00 ± 0.00	0.000	1.50 ± 0.61	0.85 ± 0.75	0.002
Total HDRS score	9.67 ± 3.51	4.33 ± 1.64	0.00	9.38 ± 2.46	3.57 ± 1.63	0.000	19.40 ± 3.79	10.25 ± 3.37	0.000

The lower the score, the milder the depression.
HDRS, Hamilton Depression Rating Scale.

The lack of familial risk in the current study was not consistent with most results indicating that the most powerful risk predictor of schizophrenia is found through genetic studies (Maki *et al.*, 2005; Walshe *et al.*, 2007).

The low familial risk in our sample could have been because of the deliberate denial of the family because of fear of stigma. Unfortunately, even genetic studies for such patients may indicate overlap between different groups as noted in Berrettnii (2000) and Crow (2008).

Phenomenology of first-episode psychosis

The results of phenomenological differences between schizophrenia spectrum patients and affective psychosis (bipolar and depression) raise three points for discussion.

(1) Differences and overlap of symptoms.
(2) Pathognomonic and points of rarity.
(3) Nosology and differential diagnosis.

Differences and overlap of symptoms

Cognitive function: the current study showed an overlap of symptoms among the three groups of patients studied. Although schizophrenia patients had significantly impaired cognitive functions, but with average intellectual abilities, that is IQ, their attention and executive functions were considerably improved after follow-up compared with affective patients.

This finding may indicate that the greater cognitive deterioration in schizophrenia could be related to the effect of illness itself and that cognitive deterioration *per se* may be responsible for the overall cognitive dysfunction in schizophrenia patients. Similar findings have been obtained in several previous studies (Bell *et al.*, 1993; Daneluzzo *et al.*, 2002; Kendell and Jablensky, 2003; Fitzgerald *et al.*, 2004; Krabbendarn *et al.*, 2005; Reichenberg *et al.*, 2009).

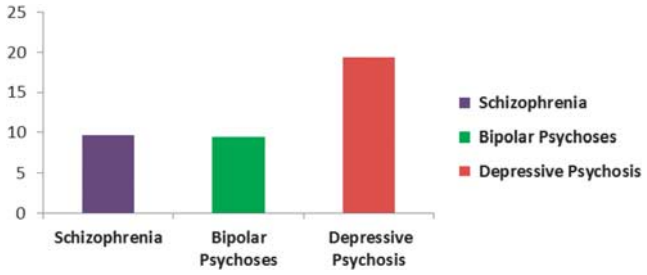
Affective symptoms: in the current study, considerable depressive and bipolar manifestations were present in the schizophrenia spectrum group. This is another indicator of an overlap of affective symptoms among patients with first-episode psychosis. Similar finding have been reported in previous studies (Sax *et al.*, 1996; Zisook *et al.*, 1999).

Psychotic symptoms: five-factor analysis and cluster analysis for PANSS indicate that our findings are consistent with previous reports showing considerable symptomatic overlap between schizophrenia and psychotic bipolar disorder, especially in the presence of positive symptoms (Pini *et al.*, 2004). Negative symptoms and anergia were found to overlap between schizophrenia and psychotic depression (Dutta *et al.*, 2007; Freudenreich *et al.*, 2008). Other symptoms such as paranoia, thought disturbances, and excitement showed overlap between schizophrenia and bipolar psychosis.

Pathognomonic and points of rarity

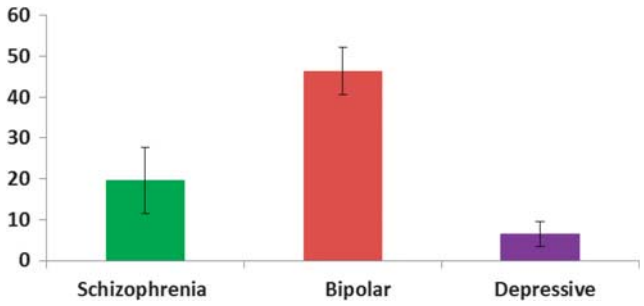
The presence of overlap and a high level of cognitive dysfunction, depression, and psychotic manifestations in all groups of patients with first-episode psychosis did not exclude the possibility of specificity of negative symptoms (Reddy *et al.*, 1992; Buchunan and Carpenter, 1994) in schizophrenia spectrum patients with first-episode psy-

Figure 3



Hamiliton Depression Rating Scale in different diagnosis of first-episode psychosis at baseline assessment.

Figure 4



Comparison of YMRS scores for different diagnoses of first-episode psychosis. YMRS, Young Mania Rating Scale.

Table 7 Comparison between baseline and end of 2 years of Young Mania Rating Scale scores for different diagnoses of first-episode psychosis

	Schizophrenia spectrum ($n=49$)			Bipolar psychosis ($n=21$)			Depressive psychosis ($n=20$)		
YMR Scale items	Baseline Mean ± SD	End of 2 years Mean ± SD	*P* value	Baseline Mean ± SD	End of 2 years Mean ± SD	*P* value	Baseline Mean ± SD	End of 2 years Mean ± SD	*P* value
1. Elevated mood	0.00 ± 0.00	0.02 ± 0.14	0.32	1.29 ± 0.72	0.81 ± 0.40	0.009	0.00 ± 0.00	0.05 ± 0.22	0.00
2. Increased motor activity	2.10 ± 1.39	0.16 ± 0.37	0.000	3.67 ± 0.48	0.86 ± 0.73	0.000	0.60 ± 0.88	0.40 ± 0.75	0.33
3. Sexual interest	0.00 ± 0.00	0.00 ± 0.00	–	1.48 ± 0.75	0.38 ± 0.50	0.000	0.00 ± 0.00	0.00 ± 0.00	0.10
4. Sleep	0.43 ± 0.65	0.12 ± 0.33	0.001	3.67 ± 0.48	0.48 ± 0.51	0.000	1.05 ± 0.51	0.90 ± 0.55	0.08
5. Irritability	2.94 ± 2.45	0.49 ± 0.74	–	7.52 ± 0.51	1.81 ± 0.41	0.000	0.40 ± 0.82	0.25 ± 0.55	0.39
6. Speech (rate and amount)	0.41 ± 0.91	0.08 ± 0.28	0.01	6.71 ± 0.46	1.57 ± 1.47	0.000	0.00 ± 0.00	0.00 ± 0.00	–
7. Language thought disorder	1.84 ± 0.92	0.98 ± 0.66	0.00	3.29 ± 0.85	0.38 ± 0.59	0.000	0.00 ± 0.00	0.00 ± 0.00	–
8. Thought content	3.88 ± 2.32	1.57 ± 0.74	0.00	7.33 ± 0.97	2.67 ± 0.48	0.000	1.50 ± 2.50	0.70 ± 1.13	0.03
9. Disruptive aggressive behavior	3.08 ± 1.67	0.65 ± 0.78	0.00	5.33 ± 0.97	0.81 ± 0.93	0.000	0.00 ± 0.00	0.00 ± 0.00	–
10. Appearance	2.16 ± 0.72	0.90 ± 0.55	0.00	2.43 ± 0.87	0.33 ± 0.48	0.000	1.75 ± 0.64	0.90 ± 0.64	0.000
11. Insight	2.8 ± 0.96	1.29 ± 0.58	0.00	3.67 ± 0.84	0.62 ± 0.50	0.000	1.20 ± 0.70	0.20 ± 0.52	0.000
Total score of YMRS	19.63 ± 8.07	6.27 ± 2.7	0.00	46.38 ± 5.72	10.62 ± 2.9	0.000	6.50 ± 3.10	3.40 ± 1.73	0.00

The lower the score, the milder the condition.
YMRS, Young Mania Rating Scale.

Table 8 Positive and Negative Syndrome Scale five-factor, cluster and total scores, and subscores for different diagnoses of first-episode psychotic patients at the baseline study point

	Schizophrenia spectrum ($n=49$)		Bipolar psychoses ($n=21$)		Depressive psychosis ($n=20$)		
	Mean	SD	Mean	SD	Mean	SD	*P*
PANSS – five-factor scores							
Positive	16.01	4.59	20.52	3.12	4.60	0.93	0.008
Negative	23.25	6.82	10.34	4.64	15.00	3.20	0.001
Depression	13.98	5.55	11.29	2.67	16.10	3.27	0.01
Cognitive disorganization	15.85	4.90	10.15	2.92	10.80	1.97	0.001
Excitement	16.14	3.92	20.19	2.69	5.25	0.55	0.003
PANSS – cluster scores							
Anergia	10.97	4.61	7.01	2.44	8.55	2.61	0.05
Thought disturbance	15.82	4.30	19.00	2.86	5.81	1.00	0.001
Paranoia	13.32	3.64	16.43	2.30	5.00	0.00	0.005
PANSS – total subscores							
Positive total	27.22	7.46	35.29	4.11	8.75	0.88	0.001
Negative total	26.98	6.79	17.41	5.12	17.44	1.82	0.04
General psychopathology	54.63	8.75	53.52	5.74	40.41	6.13	0.02
Total PANSS score	108.80	13.12	106.52	13.47	58.70	8.55	0.001

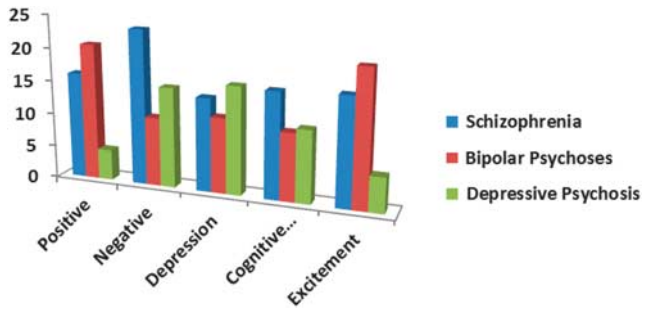
The lower the score, the milder the condition.
PANSS, Positive and Negative Syndrome Scale.

Table 9 Positive and Negative Syndrome Scale five-factors, cluster and total scores, and subscores for different diagnoses of first-episode psychotic patients at baseline and at the end of 2 years

	Schizophrenia spectrum ($n=49$)		Bipolar psychoses ($n=21$)		Depressive psychosis ($n=20$)	
	Baseline	End of 2 years	Baseline	End of 2 years	Baseline	End of 2 years
PANSS – five-factor scores						
Positive	16.01 ± 4.59	5.71 ± 2.79	20.52 ± 3.12	6.0 ± 1.94	4.60 ± 0.93	4.10 ± 0.31
Negative	23.25 ± 6.82	19.18 ± 7.91	10.34 ± 4.64	7.39 ± 2.22	15.0 ± 3.2	9.1 ± 2.35
Depression	13.98 ± 5.55	5.9 ± 2.02	11.29 ± 2.67	5.76 ± 1.0	16.10 ± 3.27	9.30 ± 2.49
Cognitive disorganization	15.85 ± 4.90	13.91 ± 4.61	10.15 ± 2.92	7.91 ± 1.4	10.80 ± 1.97	7.50 ± 1.99
Excitement	16.14 ± 3.92	4.97 ± 1.84	20.19 ± 2.69	5.33 ± 1.68	5.25 ± 0.55	4.75 ± 0.44
PANSS – cluster scores						
Anergia	10.97 ± 4.61	7.94 ± 4.36	7.01 ± 2.44	4.24 ± 0.62	8.55 ± 2.61	6.25 ± 0.99
Thought disturbance	15.82 ± 4.3	6.10 ± 2.29	19.0 ± 2.86	6.0 ± 2.10	5.8 ± 1.0	4.6 ± 0.82
Paranoia	13.32 ± 3.64	4.64 ± 2.48	16.43 ± 2.30	4.09 ± 0.95	5.0 ± 0.0	3.40 ± 0.00
PANSS – total sub scores						
Positive total scores	27.22 ± 7.46	10.04 ± 3.61	35.29 ± 4.11	10.33 ± 2.96	8.76 ± 0.88	7.55 ± 0.51
Negative total scores	26.98 ± 6.79	17.41 ± 9.36	17.71 ± 5.12	7.71 ± 0.90	17.40 ± 1.82	9.85 ± 1.63
General psychopathology scores	54.63 ± 8.75	24.73 ± 5.00	53.52 ± 5.74	21.43 ± 1.75	40.40 ± 6.13	26.00 ± 4.44
Total PANSS scores	108.80 ± 13.12	52.35 ± 11.95	106.52 ± 13.47	39.57 ± 4.04	58.70 ± 8.55	36.60 ± 6.24

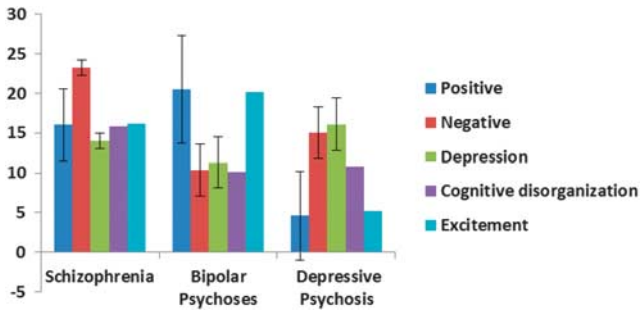
PANSS, Positive and Negative Syndrome Scale.

Figure 5



PANSS five-factor scores for different diagnoses of first-episode psychotic patients at the baseline study point. PANSS, Positive and Negative Syndrome Scale.

Figure 6



PANSS five-factor scores for different diagnoses of first-episode psychotic patients at the baseline study point. PANSS, Positive and Negative Syndrome Scale.

chosis. This was supported by the higher level of negative symptoms in schizophrenia compared with the other two groups and the lower response to treatment at the end of the study for such symptoms in schizophrenia patients.

The cognitive disorganization factor of the PANSS has some diagnostic specificity, being at a higher level in schizophrenia at baseline, with a lower response at the end of the study in comparison with affective psychosis.

Thus, cognitive disturbances might be considered an important differential diagnostic assessment of schizophrenia (Addington and Addington, 2000; Bilder *et al.*, 2000; Keele and Penton, 2007; Keefe, 2008; Barch and Keefe, 2010).

The higher level of depression in depressive psychosis and less response in the 2-year follow-up may provide an indication of the importance of the degree of depression as a differential point between psychotic depression from schizophrenia and bipolar disorders. To date, the study of first-episode unipolar depressive disorder has been limited (Strakowski *et al.*, 1998; Tohen *et al.*, 2000).

Nosology and differential diagnosis

The results, which showed an overlap between the three groups in affective, psychotic symptoms, and cognition, with some degree of specificity in negative symptoms and cognitive disorganization in schizophrenia patients, may highlight and support dimensional view or aconitum of such manifestation. This also highlights both the strength and the limitation of psychotic symptoms in the differential diagnosis of psychotic disorders early in their course.

It is important to note that the literature is mixed in the degree of specificity of neuropsychological dysfunction for schizophrenia (Bora *et al.*, 2010).

During the first episode of psychosis, the diagnostic differentiation is complex and the lack of historical data can sometimes lead to a misdiagnosis (Gonzalez-Pinto *et al.*, 1998).

A dimensional paradigm is required in order to understand the complex phenomenological manifestation of psychosis (Benabarre *et al.*, 2001; Peralta and Cuesta, 2003; Baldwin *et al.*, 2005; Peralta and Cuesta, 2007). Without laboratory tests linked to a systematic understanding of illness pathophysiology or the ability to differentiate primary and secondary symptoms, it would be difficult to determine whether the high degree of overlap of symptoms across psychotic disorders results from a high prevalence of secondary symptoms or a more fundamental problem in the model of categorically differentiated diagnostic categories for psychotic disorders that has been guided by Kraepelin's thinking.

Future work should better clarify the common and distinguishing clinical and neurobiological features of psychotic disorders ideally on the basis of differential pathophysiology; thus, the boundaries of these illnesses may be better designed. Also, work is required to clarify the conceptual model for psychotic disorder in terms of dimensional or categorical models or a combination of both.

The strength of our study is its prospective nature: the use of face-to-face interviews using structured or standardized instruments and diagnosis on the basis of frequent assessments in drug-naive sample of first-episode psychosis.

The absence of specific predictors in the current study with the lack of significance of sociodemographics, clinical characteristic, and symptom severity may limit such results, especially in the absence of neurobiological findings, for example genetic studies.

Learning about the differential phenomenological manifestations of psychotic disorder and their relevance to treatment remains an ongoing challenge for clinical studies of affective and nonaffective psychotic disorders.

Conclusion

Phenomenological differentiation of patients with first-episode psychosis is quite difficult. Combined family history, course of illness, treatment response, premorbid functions as well as phenomenological characteristic may be helpful in differentiation later in the course of illness of first-episode psychosis.

Recommendations

Future work in differentiation between primary and secondary symptoms may aid the differential diagnosis of psychosis at onset.

Researches of neurobiological findings by genetic studies and laboratory tests are important to determine points of rarity.

Review of the nosological system considering both the dimensional and the categorical paradigm may help resolve confusion both in clinical and in scientific scenarios.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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