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Diagnostic stability of first-episode psychosis and predictors of diagnostic shift from non-affective psychosis to bipolar disorder: A retrospective evaluation after recurrence ☆

Ji Sun Kim [a], Ji Hyun Baek [a], Ji Sun Choi [b], Dongsoo Lee [a], Jun Soo Kwon [c], Kyung Sue Hong [a,b,*]

[a] Department of Psychiatry, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea
[b] Samsung Biomedical Research Institute, Samsung Medical Center, Seoul, Republic of Korea
[c] Department of Neuropsychiatry, Seoul National University College of Medicine, Seoul National University Hospital, Seoul, Republic of Korea

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ABSTRACT

Diagnostic changes during follow-up are not uncommon with a first-episode psychosis (FEP). This study aimed to evaluate the diagnostic stability of the FEP and to identify factors associated with a diagnostic shift from non-affective psychosis to bipolar disorder. Considering that the diagnosis of FEP is frequently more definite after recurrence in many clinical settings, a retrospective evaluation after recurrence was preformed. Subjects were 150 patients with psychotic disorders who had been admitted to a psychiatric ward both for first episode and recurrence of their psychosis. Consensus diagnosis was made for each episode through a review of hospital records. Patients diagnosed with non-affective psychoses at the first episode were included in the analysis of predictive factors of a diagnostic shift to bipolar disorder. First-episode diagnoses were revised upon recurrence in 20.7% of patients. The most common change was to bipolar disorder accounting for more than half of all diagnostic changes. Schizophrenia exhibited the highest prospective and retrospective diagnostic consistencies. Female gender, short duration of untreated psychosis, high level of premorbid functioning, and several symptoms including lability, mood elation, hyperactivity, and delusions with religious or grandiose nature were identified as predictive factors for a diagnostic shift from non-affective psychosis to bipolar disorder. Clinical features of psychoses seem to evolve during the disease course resulting in diagnostic changes upon recurrence in a significant portion of FEP. Special consideration on a diagnostic shift to bipolar disorder is required in patients exhibiting the predictive factors identified in the current study.

1. Introduction

Diagnostic stability is regarded as a major validating factor in defining and classifying psychotic disorders (Robins and Guze, 1970; Schwartz et al., 2000). With its characteristic fluctuating symptomatology and unclear mood symptoms, first-episode psychosis (FEP) may be more vulnerable to diagnostic change over time compared to later stages of psychosis (Amini et al., 2005; Bromet et al., 2005). Accurate diagnosis at the first episode is important for planning medical and psychosocial treatments (Bromet et al., 2005; Whitty et al., 2005; Fraguas et al., 2008). In addition, diagnostic change during follow-up could influence doctor–patient rapport and patient's compliance to the treatment (Llorca, 2008).

According to previous studies on the diagnostic stability of FEP, schizophrenia and bipolar disorder show high rates of stability, even though results for other psychotic disorders are somewhat variable (Schwartz et al., 2000; Amini et al., 2005; Salvatore et al., 2009). However, the duration of follow-up in most of these prospective studies was no more than a few years which may have been too short to fully grasp the evolution of FEP clinical features. Given that diagnoses in clinical settings tend to be made more definite after recurrence (Schwartz et al., 2000), and that time to recurrence is highly variable among individual patients (Ohmori et al., 1999), diagnostic reevaluation after recurrence is needed to clarify the diagnostic stability of the FEP.

It has been argued that there are three primary diagnostic nodes in FEP, i.e., schizophrenia spectrum psychosis, bipolar disorder, and major depressive disorder with psychotic features, around which there exist additional and overlapping diagnostic categories that are distinct only in terms of their operational definition (Baldwin et al., 2005). Similarly, it has been suggested that in the early phase of psychosis, only three different diagnostic categories would be sufficient, i.e., schizophrenic spectrum type, affective psychosis, and psychotic disorder not otherwise specified (NOS) (Rahm and Cullberg,

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* Corresponding author. Department of Psychiatry, Sungkyunkwan University School of Medicine, Samsung Medical Center, #50 Irwon-Dong, Gangnam-Gu, Seoul 135-710, Republic of Korea. Tel.: +82 234103584; fax: +82 234100050.
E-mail address: hongks@skku.edu (K.S. Hong).

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2007). Considering that patients with mood disorders and those with schizophrenia spectrum disorders are likely to require different medical and psychosocial treatments (Bola et al., 2009), differentiation between these two categories would be clinically important regarding the diagnosis of FEP.

To date, follow-up studies related to FEP that investigated predictive factors of a diagnostic shift have primarily focused on schizophrenia (Schwartz et al., 2000; Jarbin and von Knorring, 2003; Schimmelmann et al., 2005; Addington et al., 2006; Haahr et al., 2008). Consistently identified risk factors for a diagnostic shift to schizophrenia from other initial diagnoses included poorer premorbid functioning and longer duration of untreated psychosis. Other studies assessed factors associated with the diagnostic shift itself regardless of the direction of change (Whitty et al., 2005; Salvatore et al., 2009). To our knowledge, no previous studies have investigated predictive factors for a diagnostic shift to affective psychoses including bipolar disorder. According to a recent large-scale follow-up study of FEP (Salvatore et al., 2009), however, change from non-affective psychosis to affective psychosis (16/191) was much more frequent than vice versa (1/308). In addition, it has been demonstrated that adolescents with psychotic mood disorders frequently present with paranoia, marked thought disorder, and behavioral deterioration. As a result, a large portion of adult bipolar diagnoses was initially diagnosed with schizophrenia at their first episode in adolescence (Werry et al., 1991; Carlson et al., 1994; McClellan and McCurry, 1999; Jarbin and von Knorring, 2003; McClellan et al., 2007). Therefore, the identification of predictive factors of subsequent diagnostic shifts to mood disorders from other psychoses might be especially intriguing for the study of FEP.

This study aimed to evaluate the diagnostic stability of FEP and to identify predictive factors associated with the diagnostic shift from non-affective psychosis to affective psychosis. Retrospective assessment was performed for patients with FEP who had been admitted to the psychiatric ward both for first episode and recurrence of their psychosis. To the best of our knowledge, this is the first report relating to the diagnostic change between first episodes and subsequent relapses of psychosis. It also represents the first investigation of the predictive factors related to the diagnostic shift to affective psychosis, and in particular, bipolar disorder.

2. Methods

2.1. Subjects

Medical records were reviewed for all patients who had been admitted at least twice to the inpatient unit of Samsung Medical Center (SMC) from October 1994 to February 2009, and diagnosed with psychotic disorders at discharge (including rule-out diagnoses) ($n=637$). Among these patients, those who had been admitted for their FEP and then readmitted for at least one relapsed psychotic episode ($n=154$) were included in the analysis. Psychotic episode was defined as having at least one psychotic symptom including delusions, hallucinations, disorganized speech, grossly disorganized, or catatonic behavior. Exclusion criteria were: (1) psychotic symptoms related to a general medical condition, substance use, organic mental disorders, or neurological illnesses including head injury; and (2) the presence of mental retardation (Wechsler Adult Intelligence Scale-tested IQ<70) or pervasive developmental disorders. Additional exclusion criteria for FEP were: (1) previous psychiatric hospitalization; and (2) prior antipsychotic medication for more than 4 weeks or until remission of the psychotic symptoms.

2.2. Procedure

Retrospective review of medical records was performed with respect to the diagnoses of first and relapsed episodes, and clinical characteristics of the first episode. The SMC is a university hospital in Seoul and all of the inpatient unit medical records were written by psychiatric residents and supervised by at least one professor of psychiatry. This institute used a standardized medical record form and its clinical diagnoses were made based on the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV). Two of the three psychiatrists (JSK, JHB, and KSH) independently diagnosed each subject based on the criteria of the DSM-IV, and of which were compared to discharge diagnoses in the medical records. Disagreement between those three diagnoses was resolved by a researcher meeting for consensus diagnosis. Ratings of clinical symptoms were independently carried out by a psychiatrist (JSK) and a research nurse (JSC) with more than 4 years of psychiatric clinical experience. The same consensus process was performed. While reviewing medical records related to the first episode, raters were blind to the patients' relapsed episode diagnoses. The DSM-IV diagnosis of patients included schizophrenia, schizophreniform disorder, schizoaffective disorder, brief psychotic disorder, bipolar disorder, major depressive disorder, and psychotic disorder not otherwise specified (NOS). We excluded from the analysis subjects having either a first-episode diagnosis of schizoaffective disorder ($n=1$) or psychotic disorder NOS ($n=3$), as these diagnoses cover heterogeneous populations exhibiting mixed natures of various diagnostic categories (Malhi et al., 2008; Salvatore et al., 2009). Ultimately, 150 subjects were included in the final analysis (Table 1). This study was approved by the institutional review board of SMC.

2.3. Clinical variables included in the analysis

Several clinical history variables were assessed from medical record relating to the first episode including the onset age of psychosis, age at first admission, duration of untreated psychosis (the time from onset of psychosis until the first admission), duration of first admission, and level of functioning during the best month of the year before admission (Global Assessment of Functioning: GAF). In addition, premorbid job or school functioning was assessed using an item from the Premorbid Adjustment Scale (PAS) (Cannon-Spoor et al., 1982), i.e., 'time employed for pay or functioning in school during a period of 3 years up to 6 months before first hospitalization', and scored using a 7-point scale from 0 ('all the time') to 6 ('never') (Table 2). Symptoms at the first psychotic episode were rated using a symptom check-list which included broad domains of psychopathologies extracted from the DSM-IV criteria, the Scale for the Assessment of Negative Symptoms (SANS) (Andreasen, 1989), the Scale for the Assessment of Positive Symptoms (SAPS) (Andreasen et al., 1995), the Brief Psychiatric Rating Scale (BPRS) (Dingemans, 1990), the Positive and Negative Syndrome Scale (PANSS) (White et al., 1997), the Young Mania Rating Scale (YMRS) (Youngstrom et al., 2002), and the Hamilton Rating Scale for Depression (HRSD) (Schwab et al., 1967) (Table 3). All of the symptom items were coded as 'present', 'absent', or 'not available'. Additionally, an evaluation was performed on the time interval between the first and the next psychotic episodes for all subjects and the time from medication discontinuation until relapse of psychosis for patients who discontinued their medication after discharge from their initial admission.

2.4. Data analysis

In the analysis of diagnostic stability, we compared the diagnosis of the first episode and that of the most recently relapsed episode for each patient, and considered two broad diagnostic categories, i.e., non-affective psychosis and affective psychosis. Non-affective psychosis included schizophrenia, schizophreniform disorder, and brief psychotic disorder, and affective psychosis included bipolar disorder and major depressive disorder. Two measures of stability were calculated for the diagnostic categories and individual diagnoses. Prospective consistency represented the proportion of subjects in a category (or diagnosis) at the first episode that retained the same diagnosis at relapsed episodes. It corresponds to a positive predictive value if the most recently relapsed episode diagnosis was the gold standard. Retrospective consistency represented the proportion of subjects in the most recently relapsed episode category (or diagnosis) who previously received the same diagnosis at the first episode, and it was conceptually similar to sensitivity.

To obtain predictors for diagnostic change from non-affective psychosis to affective psychosis, we compared clinical characteristics and symptoms of the first episode between subjects whose diagnosis shifted in this way (all of the changes were to bipolar disorder in the current analysis) and those who retained non-affective psychosis at both evaluations. Group differences were tested using the t test for parametric data, the Mann–Whitney U test for non-parametric data, and the chi-square or Fisher's exact test for categorical measures. Measures with significant difference in initial bivariate comparison were entered into a logistic regression model to identify the prediction rate of diagnostic change and factors independently associated with diagnostic change.

P values of less than 0.05 were considered statistically significant in bivariate analysis. All of the statistical analysis was done using Predictive Analytics Software (PASW) version 17.0 by SPSS for Windows software (SPSS Inc; Chicago, USA).

3. Results

The mean age and the median age of subjects at the first episode were 27.7 years (range: 13–61; S.D.: 9.5), and 26.0 years (first quartile: 20.0; third quartile: 33.0), respectively, and the male to female ratio was 0.6 ($N=58:92$). The mean interval between the first episode and the next episode was 27.1 months (range: 0.25–110; S.D.: 25.3). Of the total, 68.9% (104/150) of the patients discontinued their medication before relapse of their psychosis.

Table 1 outlines a cross-tabulation of diagnoses at the first and the most recently relapsed episodes. Among the 150 subjects analyzed, first-episode diagnoses changed in 31 patients (20.7%). Prospective consistency was higher than 80% for the two broad diagnostic

Table 1
Cross-tabulation of first episode and relapsed episode DSM-IV consensus diagnosis.

First-episode diagnosis	Total, *N*	Relapsed episode diagnosis, *N*								
		Non-affective psychosis	Schizophrenia	Schizophreniform disorder	Brief psychotic disorder	Affective psychosis	Bipolar disorder	Major depressive disorder	Schizoaffective disorder	Prospective consistency (%)[a]
Non-affective psychosis	108	89				18			1	82.4
Schizophrenia	92		84	0	0		7	0	1	91.3
Schizophreniform disorder	7		4	0	0		3	0	0	0
Brief psychotic disorder	9		1	0	0		8	0	0	0
Affective psychosis	42	4				35			3	83.3
Bipolar disorder	38		3	0	0		33	0	2	86.4
Major depressive disorder	4		1	0	0		0	2	1	50.0
Total	150	93	93	0	0	53	51	2	4	
Retrospective consistency (%)[b]		95.7	90.3	–	–	66.0	64.7	100.0		

[a] Percentage of 1st episode cases with the same diagnosis at 2nd episode.
[b] Percentage of relapsed episode cases with the same diagnosis at 1st episode.

categories, i.e., non-affective and affective psychoses. Retrospective consistency of affective psychosis (66.0%) was much lower than that of non-affective psychosis (95.7%). Of those subjects having a relapsed episode diagnosis included in affective psychosis, 33.9% (18/53) was classified as having non-affective psychosis at the first episode. Among specific DSM-IV diagnoses analyzed, schizophrenia had the highest prospective (91.3%) and retrospective (90.3%) consistencies. Bipolar disorder showed a comparable prospective consistency (86.4%), but had a much lower retrospective consistency (64.7%). Schizophreniform disorder, brief psychotic disorder, and major depressive disorder had fewer subjects, and showed low prospective and retrospective consistencies. The most frequent diagnostic shifts resulted in a diagnosis of bipolar disorder as indicated by its low retrospective consistency.

The analysis of predictors of diagnostic change focused on 18 subjects whose diagnoses had shifted from non-affective psychosis to affective psychosis. All of these shifts resulted in a diagnosis of bipolar disorder, with no shift to major depressive disorder. These patients, called the changed group were compared with 89 subjects who had remained stable with non-affective psychosis, the unchanged group, focusing on demographic and clinical characteristics (Table 2). With respect to gender, the female rate was significantly higher in the changed group ($p=0.04$). The changed group showed a significantly better premorbid functioning ($p=0.04$) and a shorter duration of untreated psychosis ($p=0.03$) as compared to the unchanged group. Additionally, the interval between treatment discontinuation after the first episode and psychosis relapse was longer in the changed group. Seven clinical symptoms ascertained at FEP significantly differentiate the two groups (Table 3). Euphoria/elated mood, lability, flight of idea, religious delusion, grandiose delusion, mannerism, and hyperactivity were more frequently observed in the changed group ($p<0.05$). Disorientation was also more likely to be observed in this group ($p=0.05$). In the regression model including 10 first-episode measures which significantly differentiated the two groups (gender, premorbid functioning, duration of untreated psychosis, and seven symptom variables), 42.9% of the diagnostic change was predicted ($\chi^2=29.0$, $p=0.001$), even though no individual variable exhibited significant independent association with diagnostic change.

4. Discussion

Diagnosing patients with FEP is complicated by the broad symptomatic overlap of various psychotic disorders and by the evolution of the illness, even though we assume reliable information gathering and measurement. Diagnostic stability and predictive factors associated with diagnostic change are important considerations in planning relevant therapeutic interventions for patients with FEP.

To obtain insight on the diagnostic stability from comprehensive follow-up data including clinical characteristics at the recurrence, we retrospectively investigated patients with psychotic disorders who had been admitted to the psychiatric inpatient unit of the SMC for both FEP and recurrence of psychosis. All of the diagnostic formulation

Table 2
Comparison of clinical characteristics between diagnosis-changed and -unchanged groups in patients with non-affective psychosis at the first episode.

	Changed to bipolar disorder ($n=18$)	Remained in non-affective psychosis ($n=89$)	Analysis	
			χ^2, *t*, *U*	*p*
Sex, male/female (%)	3/15 (16.7/83.3)	40/49 (44.9/55.1)	6.43[a]	0.04
Education, mean years (S.D.)	14.00 (2.79)	13.51 (3.03)	709.00[b]	0.43
Occupation, present/absent (%)	16/2 (88.9/11.1)	66/23 (74.2/25.8)	2.13[a]	0.35
Age of onset, years (S.D.)				
Psychotic symptom	25.56 (9.22)	26.66 (9.08)	729.00[b]	0.55
First admission	26.50 (10.00)	27.99 (9.37)	701.50[b]	0.41
Duration of untreated psychosis, months (S.D.)	12.32 (23.76)	18.14 (29.85)	547.00[b]	0.03
Duration of first admission, days (S.D.)	30.06 (11.70)	36.38 (16.21)	618.50[b]	0.23
GAF score at first admission (S.D.)	38.86 (17.09)	40.91 (14.40)	162.50[b]	0.58
Premorbid job/school functioning[c] (S.D.)	1.11 (1.49)	2.07 (1.96)	556.50[b]	0.04
Duration between first and relapsed episodes, months (S.D.)	31.39 (27.72)	27.69 (24.57)	759.50[b]	0.73
Duration between treatment discontinuation and relapse, months[d] (S.D.)	20.25 (23.67)	9.38 (19.09)	223.50[b]	0.02

Abbreviations: GAF = Global Assessment of Functioning.
[a] The χ^2 test was used.
[b] The Mann–Whitney *U* test was used.
[c] Rated on a 7-point scale from 0 ('all the time') to 6 ('never') (Cannon-Spoor et al., 1982).
[d] Subjects who discontinued their medication before the relapse were included in the analysis ($n=12$ in the changed group, $n=66$ in the remained group).

Table 3
Comparison of first-episode symptoms between diagnosis-changed and -unchanged groups in patients with non-affective psychosis at the first episode.

	Changed to bipolar disorder ($n=18$)		Remained in non-affective psychosis ($n=89$)		Analysis	
					χ^2	p
	Present, N (%)	Valid (N)	Present, N (%)	Valid (N)		
Disorientation	3(17.6)	17	3(3.4)	87	FE	0.05
Distractibility	15(83.3)	18	64(72.7)	88	FE	0.55
Blunted affect	7(43.8)	16	31(36.9)	84	FE	0.78
Inappropriate affect	10(55.6)	18	45(51.1)	88	0.12	0.73
Ambivalence	1(16.7)	6	11(37.9)	29	FE	0.64
Euphoria/elated mood	7(38.9)	18	12(13.6)	88	FE	0.02
Lability	13(76.5)	17	34(38.2)	89	8.47	0.01
Irritability	14(77.8)	18	60(70.6)	85	0.38	0.74
Aggression	11(61.1)	18	64(79.0)	81	FE	0.13
Depressive/dysphoric mood	15(83.3)	18	57(64.8)	88	2.36	0.12
Guilt	4(26.7)	15	17(27.0)	63	FE	1.00
Anhedonia	15(83.3)	18	84(94.4)	89	FE	0.44
Anxiety	15(83.3)	18	84(94.4)	89	FE	0.13
Agitation	15(88.2)	17	72(83.7)	86	FE	1.00
Fear	5(27.8)	18	16(18.6)	86	FE	0.35
Tension	13(76.5)	17	72(84.7)	85	FE	0.48
Hyperphagia	1(5.6)	18	1(1.1)	88	FE	0.31
Poor appetite	6(37.5)	16	24(30.8)	78	0.28	0.57
Hypersomnia	0(0)	18	1(1.1)	88	FE	1.00
Insomnia	13(72.2)	18	48(54.5)	88	1.91	0.20
Weight gain	0(0)	13	0(0)	71	0.00	1.00
Weight loss	2(18.2)	11	10(16.9)	59	FE	1.00
Thought Blocking	0(0)	18	17(19.5)	87	FE	0.04
Loosening of association	13(72.2)	18	59(69.4)	85	0.06	1.00
Incoherency	9(52.9)	17	46(52.9)	87	0.00	1.00
Irrelevant speech	10(55.6)	18	38(44.2)	86	0.77	0.38
Circumstantiality	9(52.9)	17	46(54.8)	84	0.02	0.89
Poverty of speech	1(5.6)	18	5(5.6)	89	FE	1.00
Pressure of speech	3(16.7)	18	7(7.9)	89	FE	0.37
Racing thought	1(5.9)	17	1(1.2)	86	FE	0.30
Flight of idea	4(23.5)	17	5(6.0)	83	FE	0.04
Thought insertion	6(46.2)	13	18(35.3)	51	FE	0.53
Thought broadcasting	4(33.3)	12	15(29.4)	51	FE	1.00
Delusion of being controlled	2(18.2)	11	18(38.3)	47	FE	0.30
Somatic delusion	3(16.7)	18	19(24.4)	78	FE	0.76
Persecutory delusion	15(88.2)	17	82(92.1)	89	FE	0.63
Delusion of infidelity	0(0)	18	8(9.3)	86	FE	0.35
Erotic delusion	2(11.1)	18	12(13.8)	87	FE	1.00
Religious delusion	6(33.3)	18	9(10.5)	86	FE	0.02
Grandiose delusion	8(50.0)	16	15(18.5)	81	FE	0.02
Delusion of poverty	0(0)	18	1(1.1)	88	FE	1.00
Idea of reference	13(81.3)	16	75(89.3)	84	FE	0.40
Obsession	1(6.3)	16	10(13.9)	72	FE	0.68
Preoccupation	18(100)	18	82(95.3)	86	FE	1.00
Hypochondriasis	3(17.6)	17	13(15.1)	86	FE	0.73
Suicidal idea	5(29.4)	17	24(27.6)	87	FE	1.00
Auditory hallucination	12(70.6)	17	46(52.3)	88	1.93	0.16
Visual hallucination	5(31.3)	16	15(17.9)	84	FE	0.30
Tactile hallucination	0(0)	17	3(3.4)	88	FE	1.00
Olfactory hallucination	0(0)	18	3(3.4)	88	FE	1.00
Gustatory hallucination	0(0)	18	0(0)	88	0.00	1.00
Catatonia	0(0)	18	7(7.9)	89	FE	0.60
Bizarre behavior	16(88.9)	18	75(84.3)	89	FE	1.00
Stereotypy	2(11.1)	18	3(3.4)	88	FE	0.20
Mannerism	2(11.1)	18	0(0)	87	FE	0.03
Self mutilation	2(11.1)	18	6(6.7)	89	FE	0.62
Excitement	13(76.5)	17	63(72.4)	87	FE	1.00
Negativism	1(5.6)	18	7(7.9)	89	FE	1.00
Mutism	1(5.6)	18	5(5.7)	88	FE	1.00
Hyperactivity	5(27.8)	18	6(6.8)	88	FE	0.02
Hypersexuality	2(11.1)	18	7(8.1)	86	FE	0.65
Impulsivity	16(100)	16	69(85.2)	81	FE	0.21
Compulsion	1(5.9)	17	4(5.1)	79	FE	1.00
Hypoactivity	0(0)	18	8(9.0)	89	FE	0.35
Anergia	1(5.6)	18	4(4.8)	84	FE	1.00
Avolition	3(16.7)	18	21(24.1)	87	FE	0.76
Social withdrawal	9(50.0)	18	56(64.4)	87	1.31	0.29
Poor rapport	6(33.3)	18	36(42.4)	85	0.50	0.60
Uncooperativeness	10(55.6)	18	52(59.8)	87	0.11	0.80
Poor insight	16(94.1)	17	84(94.4)	89	FE	1.00
Disturbances of abstract thinking	7(53.8)	13	42(62.7)	67	0.36	0.55

Abbreviations: FE = Fisher's exact test.

was performed based on DSM-IV classification and criteria. We excluded schizoaffective disorder and psychotic disorder NOS from the initial diagnosis considering the ambiguity of criteria for these diagnoses.

With those formulated at recurrence, 79.3% of the first-episode diagnoses were consistent. This rate is comparable to or slightly higher than those generated from previous prospective follow-up studies of FEP (72.0%–77.6%) (Schwartz et al., 2000; Salvatore et al., 2009; Whitty et al., 2005). Given that both baseline characteristics of subjects and evaluation methods have differed between studies, interpretation of their variable results would be complicated and beyond the scope of the current study. In this study, schizophrenia and bipolar disorder as individual diagnosis, and non-affective and affective psychoses as diagnostic categories exhibited prospective diagnostic stability of higher than 80.0% (82.4–91.3%). However, retrospective stability was relatively low for bipolar disorder (64.7%) indicating a noticeable diagnostic shift to this diagnosis at recurrence.

In the analyses of diagnostic change, the main shift was that of bipolar disorder ($n=18$) from non-affective psychoses accounting for more than half of all diagnostic changes ($n=31$). Further, 16.7% of initial non-affective cases were diagnosed as having affective psychosis (specifically bipolar disorder) at the recurrence, whereas 9.5% of initial affective disorders were later diagnosed with non-affective psychosis (specifically schizophrenia). This result is in line with that of a recent large-scale prospective study of FEP (Salvatore et al., 2009). Even though the authors of that study focused more on a high shift rate to schizoaffective disorder (24.1%) in initial non-affective cases, their data also revealed a much higher rate of change from non-affective psychosis to affective psychosis (16/191 = 8.4%) compared to the reverse (1/308 = 0.32%). In the current study, those initial diagnoses which had shifted to bipolar disorder included schizophrenia, schizophreniform disorder and brief psychotic disorder. Even though the latter two conditions are acute illnesses, which one would expect to have their diagnoses changed at recurrence, the diagnostic change to bipolar disorder implies the evolution of clinical features resulting in an increased manifestation of clear affective symptoms. In addition, 7.6% of initial diagnoses of schizophrenia, which had required six continuous months of illness in order to meet the DSM-IV criteria, had changed to bipolar disorder at recurrence. These results suggest that consideration of the misidentification of bipolar disorder as schizophrenia spectrum disorders in the early stages of psychoses should not be confined to adolescent patients.

In regard to predictive factors associated with diagnostic change, we focused on the differentiation of subjects who were shifted to bipolar disorder from those who remained as non-affective psychoses. Better premorbid job/school functioning and shorter duration of untreated psychosis were associated with the diagnostic shift. Even though there have been no comparable studies investigating predictive factors for a shift from non-affective to affective psychoses, worse premorbid functioning and longer duration of untreated psychosis were reported to be risk factors for diagnostic change to schizophrenia from other initial diagnoses (Schwartz et al., 2000; Schimmelmann et al., 2005; Addington et al., 2006; Haahr et al., 2008).

Among clinical symptoms appearing before or during the admission of patients with FEP, an elated or labile mood, hyperactivity, flight of idea, disorientation, and delusions with religious or grandiose nature were associated with the diagnostic shift to bipolar disorder. Special consideration of the possibility of a bipolar disorder diagnosis seems to be required in cases of FEP exhibiting these symptoms even though patients may not have met the diagnostic criteria for mood episodes. Results also indicated that female FEP patients were more vulnerable to diagnostic change to bipolar disorder from non-affective psychoses. Further, time to relapse after discontinuation of medication was much longer in patients whose diagnosis were changed to bipolar disorder as compared to the unchanged group.

The present study had certain limitations that require consideration in the interpretation of data. First, subjects were limited to patients who had experienced a recurrence of psychosis and had been admitted to the hospital both for initial and recurred episodes. Therefore, generalization of these results to patients with milder psychotic episodes or to those without recurrence for a long period of time may be limited. Second, retrospective reevaluation of medical records described by a number of different clinicians may be biased to varying degrees with respect to chart quality and clinician qualifications. As a compromise, all assessments in the current study were independently performed by two individual raters followed by consensus rating processes. In addition, raters were blind to the diagnosis of the relapsed episode while evaluating the FEP. The third limitation is related to the use of a relatively small sample size for several diagnostic categories reflecting their limited prevalence among our cohort. Such power limitation precluded statistical analysis of predictive factors for specific diagnostic changes. Specifically, it was hard to analyze risk factors for diagnostic shifts from major depressive disorders or individual diagnoses included in non-affective psychoses to bipolar disorder.

In contrast, this study includes two main strengths. First, we evaluated the diagnostic shift and predictive factors based on comprehensive information gathered until the time of recurrence. Given that clinical diagnoses of psychotic episodes could become clearer after the recurrence, short-term follow-up studies may not fully capture the evolution of disease processes. In fact, the interval between the first and the next episode was up to 9 years (average 27.1 months) in our subjects, illustrating the length of follow-up required. Second, even though direct interviews were not performed in the current study, medical records for the subjects included information gathered through continuous assessment by a therapist team throughout the hospitalization period (average of one month).

In summary, more than one-fifth of the patients who presented with FEP were given a different diagnosis upon recurrence. The most common change was to a diagnosis of bipolar disorder from original diagnoses of schizophrenia, schizophreniform disorder, and brief psychotic disorders. Female gender, shorter duration of untreated psychosis, higher level of premorbid functioning, and several clinical symptoms including manic mood symptoms were identified as predictive factors for a diagnostic shift from non-affective psychosis to bipolar disorder. The present study suggests that the clinical features of FEP evolve over the disease course and that a rigid adherence to DSM-IV requirements may lead to an under diagnosis of initial bipolar disorder.

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