Occurrence and Clinical Correlates of Psychiatric Comorbidity in Patients With Psychotic Disorders

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Background: The aim of this study was to explore patterns and clinical correlates of psychiatric comorbidity in patients with schizophrenia spectrum disorders and mood spectrum disorders with psychotic features.

Method: Ninety-six consecutively hospitalized patients with current psychotic symptoms were recruited and included in this study. Index episode psychotic diagnosis and psychiatric comorbidity were assessed using the Structured Clinical Interview for DSM-III-R-Patient Version (SCID-P). Psychopathology was assessed by the SCID-P, Brief Psychiatric Rating Scale, Scale for the Assessment of Negative Symptoms, and Hopkins Symptom Checklist. Awareness of illness was assessed with the Scale to Assess Unawareness of Mental Disorders.

Results: The total lifetime prevalence of psychiatric comorbidity in the entire cohort was 57.3% (58.1% in schizophrenia spectrum disorders and 56.9% in mood spectrum psychoses). Overall, panic disorder (24%), obsessive-compulsive disorder (24%), social phobia (17.7%), substance abuse (11.5%), alcohol abuse (10.4%), and simple phobia (7.3%) were the most frequent comorbidities. Within the group of mood spectrum disorders, negative symptoms were found to be more frequent among patients with psychiatric comorbidity than among those without comorbidity, while such a difference was not detected within the group of schizophrenia spectrum disorders. Social phobia, substance abuse disorder, and panic disorder comorbidity showed the greatest association with psychotic features. An association between earlier age at first hospitalization and comorbidity was found only in patients with unipolar psychotic depression. Patient self-reported psychopathology was more severe in schizophrenia spectrum patients with comorbidity than in those without, while such a difference was less pronounced in mood spectrum psychoses.

Conclusion: These findings suggest that psychiatric comorbidity is a relevant phenomenon in psychoses and is likely to negatively affect the phenomenology of psychotic illness. Further studies in larger psychotic populations are needed to gain more insight into the clinical and therapeutic implications of psychiatric comorbidity in psychoses.

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Psychiatric comorbidity, defined as the co-occurrence of one or more psychiatric disorders with a principal diagnosis, has been primarily investigated in affective and anxiety disorders where it was observed to affect severity, course, and treatment response.[1–6]

Psychiatric comorbidity in schizophrenia spectrum disorders or mood spectrum disorders with psychotic features has been less investigated for the following reasons: (1) the adoption of operationalized diagnostic criteria has consolidated the assumption that any concomitant psychiatric disorder that is hierarchically lower than the principal diagnosis may not require an adjunctive diagnosis; (2) concomitant DSM-III-R Axis I disorders with psychosis—with the exception of substance abuse disorders—may represent a nonspecific by-product of psychosis rather than distinct co-occurring conditions; (3) the validity of multiple diagnoses in psychoses may be questionable because of the presence of several confounding factors, such as symptom overlapping between psychosis and comorbid disorder, effects of treatments on psychopathology, and information bias.

Nevertheless, recent epidemiologic studies conducted in the general population have shown that psychiatric comorbidity among subjects with psychotic disorders is a substantial phenomenon, with an overall prevalence higher than 58%.[7] Previous findings on comorbidity in psychoses essentially derive from a few studies conducted in clinical samples. Strakowski et al.,[8] for example, found a total lifetime prevalence of psychiatric comorbidity of 40.2%. Substance abuse and alcohol abuse were significantly more frequent among affective (28.0%) than nonaffective psychoses (7.4%). Prevalence of psychiatric comorbidity in bipolar disorder with psychotic features was found to range between 13% and about 40%, with alcohol or substance abuse disorders usually being the most common conditions, followed by antisocial personality, anxi-

ety disorders, delirium, and dementia.[9–11] Panic disorder was also found to be frequently associated with psychotic mania with a prevalence of 24.4%.[12]

Psychotic patients with psychiatric comorbidity were found to have a greater length of hospital stay, lower rate of recovery at discharge, and a worse response to somatic treatment than those without comorbidity.[8–10] Siris et al.[13–15] found that treatment of depression in the course of schizophrenia may help to prevent subsequent psychotic exacerbation or relapse. As to mood disorders, it has been argued that the clinical profile of manic patients with other comorbid psychiatric disorders is atypical and resembles the neurotic secondary depression described by Winokur et al.[9,16]

These findings suggest that psychiatric comorbidity may have an impact on psychosis and pose questions on whether psychotic patients with a history of other psychiatric disorders might have different clinical and psychopathologic characteristics compared to those without comorbidity.

The present study aims at exploring the occurrence of DSM-III-R[17] Axis I disorders in a sample of consecutively hospitalized patients with schizophrenia spectrum disorders and mood spectrum disorders with psychotic features. Secondly, we investigated the relationship between psychiatric comorbidity and type and severity of formal psychotic symptoms, namely delusions, hallucinations, behavioral abnormalities, and negative symptoms, and patient's self-reported psychopathology and age at first hospitalization.

METHOD

The patients in this study were recruited within the framework of the University of Pisa Comorbidity in Psychosis Project, an ongoing follow-up study started in April 1995 at the Institute of Psychiatry of the University of Pisa, Pisa, Italy. The Pisa center specializes in the treatment of anxiety and mood disorders and receives patients who reside in different areas of the country. Patients with alcohol dependence or substance abuse disorders are not usually admitted in the Pisa center but are referred to other specialized centers.

Ninety-six consecutively hospitalized psychotic patients were recruited and included in the study on the basis of the following criteria: (1) age over 16 years; (2) presentation with psychotic symptoms (i.e., formal thought disorders, delusions, hallucinations, grossly disorganized behavior); (3) provision of informed consent. Patients were selected independently of previous hospitalizations and/or prior antipsychotic or mood-stabilizer treatments and independently of having had a single episode or multiple episodes of psychosis. Patients were excluded from the study if psychotic symptoms (1) were secondary to acute intoxication or withdrawal from alcohol or other substances or (2) were presenting with concomitant severe medical conditions defined, according to Black et al.,[9] as any serious or acute life-threatening illness such as cancer, myocardial infarction, etc.

The inclusion diagnosis of psychosis was made by three senior psychiatrists, who were not directly involved in the study, on the basis of their clinical judgment and revision of patient records. All patients included in the study were assessed in the week preceding their discharge by the Structured Clinical Interview for DSM-III-R-Patient Version (SCID-P),[18] which generates both Axis I principal diagnosis and comorbid psychiatric diagnoses. The SCID-P has been found to facilitate DSM-III-R-based psychiatric diagnoses and covers the major Axis I disorders. Furthermore, the SCID-P tends to prompt the interviewer to assess specific symptomatology and guides patients to describe symptoms in the most detailed fashion. The SCID-P has established validity as an instrument to assess psychiatric comorbidity.[19] The index episode diagnosis was defined a priori as a psychotic disorder regardless of any associated comorbid psychiatric diagnosis. According to previous studies, psychiatric comorbidity has been defined as the presence of antecedent or concurrent DSM-III-R Axis I diagnosis in addition to the principal diagnosis of psychotic disorder. The SCID-P hierarchy was maintained for the psychotic disorder diagnosis but not for the comorbid diagnosis except for generalized anxiety disorder, which is difficult to assess in psychotic patients. For patients with mood spectrum psychosis, dysthymia was not considered comorbid unless full criteria for dysthymia had been fulfilled more than 1 year before the onset of the psychotic episode.

The SCID-P interviews were performed by three residents in psychiatry, after training for the use of the SCID-P. As recommended, SCID-P interviewers were skilled clinical researchers with at least 3 years of clinical experience and with substantial familiarity with DSM-III-R criteria.[19] In completing the SCID-P, information was obtained from any source available in addition to the patient interview, including medical records, first-degree relatives, and treating clinicians. Each patient's interview took about 4 hours to be completed. Syndromes clearly secondary to the principal psychotic illness were not rated as comorbid disorders by interviewers. This is the case, for example, of marked social phobic or obsessive-compulsive symptoms due to social or cognitive impairment determined by the principal psychotic illness. Age at onset of principal psychotic diagnosis and comorbid diagnoses were investigated by the SCID-P. Comorbid diagnoses were defined as antecedent if patients endorsed full syndrome criteria more than 1 year before the onset of the principal psychotic disorder.

Of the entire cohort of 96 psychotic patients, 31 were categorized with schizophrenia spectrum disorders (schizophrenia = 10, schizophreniform = 1, schizoaffec-

tive = 11, delusional disorder = 9) and 65 with mood spectrum disorders with psychotic features (bipolar disorder = 47, unipolar depression = 18), according to the DSM-III-R criteria. Comparisons among subgroups were also performed using a narrower definition of schizophrenia spectrum disorders (N = 22) that excluded delusional disorder from such a group. Psychopathology and symptom severity were assessed using the 18-item version of the Brief Psychiatric Rating Scale (BPRS),[20] the Hopkins Symptom Checklist (SCL-90),[21] and the Clinical Global Impressions scale (CGI),[22] respectively. Positive symptoms of psychosis were assessed using appropriate items contained in the SCID-P. Negative symptoms were assessed by the Scale for the Assessment of Negative Symptoms (SANS).[23] The assessment of lifetime psychopathology was carried out as carefully as possible, by using information provided not only by the patients but also by their first-degree relatives and previous medical records. The psychopathologic self-report assessment as obtained by the SCL-90 has provided consistent information with the interviewer-based assessment as obtained by BPRS and SANS and SCID-P items. This allowed us to be confident about the validity of our findings.

The awareness of illness was evaluated using the Scale to Assess Unawareness of Mental Disorders (SUMD).[24] The SUMD consists of six general items rated on the basis of direct patient interview on a 5-point scale for each item (from 0 = completely aware to 5 = completely unaware) and four subscales to assess insight for specific symptoms. In this study, analyses were limited to the first three general items of the SUMD (1 = awareness of mental disorder, 2 = awareness of treatment efficacy, 3 = awareness of social consequences of mental illness) concerning current episode of illness.

Information on psychiatric family history of the patient was obtained using a modified version of the Family History Method for Research Diagnostic Criteria.[25] Current pharmacologic treatments were monitored on a weekly basis and reported in appropriate forms.

An interrater reliability for the SCID-P, BPRS, SANS, and SUMD was assessed in a small sample study (N = 8) on the basis of joint records for both principal and comorbid diagnoses. Good reliability established from joint ratings was obtained for both principal and comorbid diagnoses (kappa = 0.87 and 0.82, respectively).

Statistical Analyses

The mean values of continuous variables such as age and scale scores were compared between groups using the t test for independent samples. The excess risk of having comorbid diagnoses in mood spectrum versus schizophrenia spectrum psychoses was estimated using crude odds ratios (ORs), with 95% confidence intervals (CIs). Analogously, the strength of association between individual psychotic symptoms and specific comorbid disorders was quantified in terms of crude odds ratios. Multivariate analyses were used as follows: the relationship between psychiatric comorbidity, principal psychotic diagnoses, and continuous dependent variables (SCL-90, BPRS, and SANS scores) was analyzed by fitting a separate multiple linear regression model to each scale. To study the relationship between psychiatric comorbidity and categorical dependent variables (delusions, hallucinations, behavioral symptoms), multiple logistic regression analyses were performed. For these last analyses, comorbid psychiatric diagnoses were collapsed into three categories: anxiety disorders (panic disorder, obsessive-compulsive disorder, social phobia, simple phobia), substance abuse disorders (alcohol and drug abuse disorders), and other disorders (eating disorders, hypochondriasis). All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS, Version 7.0, for Windows 95).[26]

RESULTS

In the overall sample, the mean age was 33.9 ± 10.2 years, and 54 (56.3%) were females. Sixty-one subjects (63.5%) were not married and 14 (14.6%) were separated or divorced, while 40 (35.4%) of the patients were unemployed. Eighty-seven (91%) of the sample had a medium/high educational level (8 years of school or more). Forty-eight patients were at their first hospitalization, while the other 50% of the sample had two or more previous hospitalizations. Patients at first hospitalization were significantly younger than multiply hospitalized patients (28.5 ± 7.1 and 39.4 ± 9.9 years, respectively, $t = -6.15$, $df = 94$, $p < .001$).

When the above sociodemographic characteristics were analyzed separately in schizophrenia spectrum and mood spectrum psychotics, married subjects were 16.1% (5/31) of the schizophrenia spectrum and 26.2% (17/65) of the mood spectrum psychoses, while unemployed subjects were 54.8% (17/31) and 61.5% (40/65), respectively. First hospitalization occurred earlier in schizophrenia spectrum patients (23.8 ± 6.8 years) than in mood spectrum psychotics (26.4 ± 7.4 years); this difference only approached statistical significance. First admission took place for 54.8% (17/31) of the schizophrenia spectrum group and for 47.7% (31/65) of the mood spectrum psychotics. Age at onset of principal psychotic diagnosis was found to be 22.1 ± 6.2 years in schizophrenia spectrum disorders, 23.8 ± 7.1 years in bipolar disorder, and 23.0 ± 5.2 years in unipolar depression.

One or more comorbid psychiatric diagnoses were found in 57.3% (N = 55) of the entire cohort. Of these, 32.3% (N = 31) had more than two comorbid diagnoses. No significant differences of sex, education, and employment status were found between patients with comorbidity and those without comorbidity. Overall, patients with

psychiatric comorbidity were younger (33.6 ± 9.6 years) than those without comorbidity (34.4 ± 11.0 years), but the difference did not reach significance. First hospitalization was found to be earlier among subjects with psychiatric comorbidity (26.2 ± 6.0 years), as compared to those without (29.4 ± 3.0 years), but only among patients with psychotic unipolar depression ($p < .05$, Fisher's exact test).

Self-reported psychopathology, as assessed by the SCL-90, was found to be more severe among patients with comorbidity than those without (total score = 127.2 ± 49.0 vs. 94.9 ± 66.0, $t = -2.72$, $df = 93$, $p = .008$); among the nine SCL-90 subscales, scores for obsessive/compulsivity (1.73 vs. 1.19, $p < .01$), interpersonal sensitivity (1.48 vs. 0.98, $p < .002$), depression (1.60 vs. 1.22, $p < .02$), anxiety (1.54 vs. 1.16, $p < .02$), paranoid ideation (1.56 vs. 1.12, $p < .01$) and psychoticism (1.37 vs. 1.05, $p < .04$) were significantly higher in comorbid subjects than in subjects without comorbidity. The BPRS total score was only slightly higher in subjects with comorbidity but not statistically significant (38.6 ± 10.3 vs. 35.8 ± 10.3, respectively). The SANS total score and the SANS subscale scores showed no differences between patients with and without comorbidity.

Patients with psychiatric comorbidity were significantly more likely than those without comorbidity to have good awareness of current episode of illness (OR = 5.04, 95% CI = 1.98 to 12.95), treatment efficacy (OR = 6.47, 95% CI = 2.50 to 16.72), and social consequences of their illness (OR = 4.67, 95% CI = 1.86 to 11.70) at the time of discharge.

The frequencies of psychotic symptoms (see Table 2) did not significantly differ between patients with and without comorbidity, with the exception of loss of association, which was less frequent among subjects with psychiatric comorbidity (OR = 0.33, 95% CI = 0.11 to 0.98).

As shown in Table 1, prevalence rates of Axis I comorbidities in the three main groups of psychotics did not significantly differ from each other, with the exception of anorexia nervosa, which was found to be more frequent among unipolar depressives than bipolar patients (Fisher's exact test, $p < .05$).

Panic disorder was significantly more frequent among patients with delusional disorder (Fisher's exact test, $p < .05$) or mood spectrum disorders (Fisher's exact test, $p < .04$) than schizophrenic or schizoaffective patients. No cases of social phobia were associated with a diagnosis of delusional disorder.

Schizophrenia Spectrum Versus Mood Spectrum Disorders

Frequencies of specific types of delusions, hallucinations, and behavioral symptoms did not significantly differ in schizophrenia spectrum disorders as compared to mood spectrum disorders with psychotic features, nor did awareness of current episode of illness (2.70 ± 1.49 vs. 2.44 ± 1.53), awareness of treatment efficacy (2.46 ± 1.8 vs. 2.35 ± 1.47) and awareness of social consequences of illness (2.50 ± 1.9 vs. 2.34 ± 1.66).

As shown in Table 2, psychotic phenomenology was investigated separately in patients with schizophrenia spectrum disorders (N = 31) and mood spectrum disorders (N = 65) with psychotic features with or without comorbidity. Comparisons within the schizophrenia spectrum subgroup showed that somatic delusions were more frequent among those with comorbidity (Kendall's tau test, $p < .05$), while delusions of control were more frequent in subjects without comorbidity (Kendall's tau test, $p < .05$). Frequency of hallucinations and of other behavioral symptoms did not differ between subjects with and without comorbidity.

As shown in Table 3, among schizophrenia spectrum disorders, the BPRS total score and the SANS scores did not significantly differ between patients with and without comorbidity. Only the BPRS subscale anxiety-depression score was significantly higher among patients with psychiatric comorbidity. As to SCL-90, total score and four subscale scores were significantly higher in those with comorbidity than without. When comparisons were performed excluding the 9 patients with delusional disorder from the schizophrenia spectrum group, no significant

Table 1. Lifetime Prevalence of DSM-III-R Axis I Comorbidity in 96 Consecutively Hospitalized Patients With Psychotic Disorders

DSM-III-R Axis I Comorbidity	Schizophrenia Spectrum Disorders[a] (N = 31)		Mood Spectrum Disorders With Psychotic Features: Bipolar Disorder (N = 47)		Mood Spectrum Disorders With Psychotic Features: Unipolar Depression (N = 18)		Total (N = 96)	
	N	%	N	%	N	%	N	%
Psychiatric comorbidity, total	18	58.1	25	53.2	12	66.6	55	57.3
Two or more comorbid disorders	9	29.0	14	29.8	8	44.4	31	32.3
Only one comorbid disorder	9	29.0	11	23.4	4	22.2	24	25.0
Panic disorder	6	19.4	12	25.5	5	27.8	23	24.0
Obsessive-compulsive disorder	9	29.0	10	21.3	4	22.2	23	24.0
Social phobia	5	16.1	5	10.6	7	38.9	17	17.7
Substance abuse/dependence	3	9.7	6	12.8	2	11.1	11	11.5
Alcohol abuse/dependence	2	6.5	6	12.8	2	11.1	10	10.4
Simple phobia	1	3.2	3	6.4	3	16.7	7	7.3
Past depression	6	19.4	…	…	…	…	6	6.3
Anorexia	1	3.2	1	2.1	3	16.7	5	5.2
Bulimia	0	0	2	4.2	0	0	2	2.1
Hypochondriasis	1	3.2	0	0	1	5.6	2	2.1
Agoraphobia	0	0	1	2.1	0	0	1	1.0
Dysthymia	…	…	0	0	1	5.6	1	1.0

[a]Includes schizophrenia (N = 10), schizophreniform disorder (N = 1), schizoaffective disorder (N = 11), delusional disorder (N = 9).

Table 2. Psychotic Symptomatology in Patients With Schizophrenia Spectrum Disorders and Mood Spectrum Disorders With Psychotic Features With or Without Psychiatric Comorbidity

	Psychiatric Comorbidity in Schizophrenia Spectrum Disorders[a]					Psychiatric Comorbidity in Mood Spectrum Disorders With Psychotic Features[b]				
	Absent (N = 13)		Present (N = 18)			Absent (N = 28)		Present (N = 37)		
Characteristic	N	%	N	%	p Value	N	%	N	%	p Value
Delusions[c]										
Reference	7	53.8	10	55.6	.59	21	75.0	25	67.6	.71
Persecutory	6	46.2	12	66.7	.52	22	78.6	24	64.9	.91
Grandiose	3	23.1	3	16.7	.86	11	39.3	9	24.3	.20
Somatic	0	0	4	22.2	< .05	5	17.9	5	13.5	.84
Thought broadcasting	1	7.7	2	11.1	.65	5	17.9	6	16.2	.74
Systematized	5	38.5	9	50.0	.51	8	28.6	14	37.8	.21
Guilt	2	15.4	3	16.7	.45	4	14.3	13	35.1	< .05
Control	3	23.1	1	5.6	< .05	4	14.3	5	13.5	.57
Bizarre	1	7.7	5	27.8	.21	4	14.3	6	16.2	.67
Hallucinations[c]										
Auditory	8	61.5	11	61.1	.94	18	64.3	18	48.6	.40
Visual	2	15.4	3	16.7	.47	6	21.4	13	35.1	.27
Tactile	0	0	1	5.6	.39	1	3.6	2	5.4	.93
Gustative	1	7.7	1	5.6	.79	2	7.1	6	16.2	.27
Other psychotic symptoms[c]										
Affective inappropriate	0	0	1	5.6	.28	2	7.1	3	8.1	.72
Affective flattening	4	30.8	2	11.1	.34	3	10.7	9	24.3	< .05
Catatonia	1	7.7	1	5.6	.79	1	3.6	6	16.2	< .05
Incoherence	1	7.7	3	16.7	.76	1	3.6	0	0	< .05
Loss of associations	1	7.7	2	11.1	.63	2	7.1	0	0	< .05

[a]Includes schizophrenia, schizophreniform disorder, schizoaffective disorder, delusional disorder.
[b]Includes bipolar disorder with psychotic features, unipolar depression with psychotic features.
[c]Assessed by the Structured Clinical Interview for DSM-III-R-Patient Version.

Table 3. BPRS, SANS, SUMD, and SCL-90 Mean ± SD Scores in Schizophrenia Spectrum Disorders and Mood Spectrum Disorders With Psychotic Features With and Without Psychiatric Comorbidity*

	Psychiatric Comorbidity in Schizophrenia Spectrum Disorders[a]			Psychiatric Comorbidity in Mood Spectrum Disorders With Psychotic Features[b]		
Total Score and Factor Scores	Absent (N = 13)	Present (N = 18)	t Test	Absent (N = 28)	Present (N = 37)	t Test
BPRS total score	35.70 ± 10.10	37.30 ± 11.20	NS	35.89 ± 10.60	39.32 ± 10.20	NS
Anxiety/depression	1.54 ± 0.62	2.40 ± 1.02	< .05	2.19 ± 1.15	3.03 ± 1.42	< .05
Anergia	1.77 ± 0.69	2.00 ± 1.17	NS	1.80 ± 1.13	2.28 ± 1.16	< .05
Thought disturbances	2.60 ± 1.05	2.28 ± 1.05	NS	2.36 ± 1.07	1.90 ± 0.76	NS
Activation	1.72 ± 0.90	1.59 ± 0.52	NS	1.63 ± 0.64	1.59 ± 0.57	NS
Hostility/suspiciousness	2.28 ± 1.56	1.93 ± 1.03	NS	1.87 ± 0.82	1.90 ± 0.89	NS
SANS total score	45.6 ± 30.3	33.8 ± 33.7	NS	21.21 ± 22.7	36.97 ± 22.8	< .01
Affective flattening	1.6 ± 1.6	1.1 ± 1.5	NS	0.68 ± 0.9	1.35 ± 1.2	< .05
Alogia	1.8 ± 1.5	1.1 ± 1.4	NS	0.70 ± 1.2	1.20 ± 1.1	< .05
Abulia/apathia	2.3 ± 1.2	1.8 ± 1.2	NS	1.30 ± 1.3	1.97 ± 1.3	< .05
Anhedonia/asociality	2.2 ± 1.8	1.7 ± 0.4	NS	0.95 ± 1.2	1.85 ± 1.2	< .01
Attention	1.4 ± 1.5	1.4 ± 0.3	NS	0.73 ± 1.0	0.97 ± 1.2	NS
SUMD score						
Awareness of mental disorder	4.13 ± 1.46	2.13 ± 1.41	< .01	3.04 ± 1.53	1.94 ± 1.37	< .01
Awareness of treatment efficacy	4.13 ± 1.46	1.63 ± 1.45	< .001	2.93 ± 1.61	1.88 ± 1.17	< .01
Awareness of social consequences	4.25 ± 1.49	1.63 ± 1.45	< .001	2.79 ± 1.75	1.97 ± 1.51	NS
SCL-90 total score	84.00 ± 42.00	134.30 ± 74.60	< .05	99.68 ± 51.70	123.81 ± 62.60	NS
Somatization	0.79 ± 0.48	1.23 ± 1.07	NS	0.99 ± 0.62	1.20 ± 0.72	NS
Obsessive/compulsivity	1.08 ± 0.55	1.87 ± 1.02	< .01	1.24 ± 0.77	1.65 ± 0.88	< .05
Interpersonal sensitivity	0.93 ± 0.58	1.64 ± 1.03	< .05	0.99 ± 0.62	1.39 ± 0.91	< .05
Depression	1.00 ± 0.48	1.58 ± 0.97	< .05	1.32 ± 0.71	1.60 ± 0.87	NS
Anxiety	0.95 ± 0.65	1.55 ± 0.82	< .05	1.25 ± 0.82	1.53 ± 0.89	NS
Anger/hostility	0.86 ± 0.77	1.25 ± 1.16	NS	0.85 ± 0.59	0.88 ± 0.63	NS
Phobic anxiety	0.62 ± 0.58	0.88 ± 0.75	NS	0.68 ± 0.57	1.12 ± 0.88	< .05
Paranoid ideation	1.19 ± 0.91	0.91 ± 0.98	NS	1.10 ± 0.62	1.44 ± 0.90	NS
Psychoticism	0.94 ± 0.58	1.49 ± 0.82	NS	1.10 ± 0.72	1.31 ± 0.82	NS

*BPRS = Brief Psychiatric Rating Scale, SANS = Scale for the Assessment of Negative Symptoms, SCL-90 = Hopkins Symptom Checklist, SUMD = Scale to Assess Unawareness of Mental Disorders.
[a]Includes schizophrenia, schizophreniform disorder, schizoaffective disorder, delusional disorder.
[b]Includes bipolar disorder with psychotic features, unipolar depression with psychotic features.

Table 4. Bivariate Associations (Odds Ratios) Between Specific Comorbid Diagnoses and Psychotic Features in the Entire Cohort (N = 96)*

Psychotic Feature	Panic Disorder	OCD	Social Phobia	Simple Phobia	Eating Disorders	Alcohol Abuse Disorders	Substance Abuse Disorder	More Than Two Comorbid Disorders	Females
Somatic delusions	1.91	0.87	3.48[a]	0.94	0.94	1.50	4.17[a]	1.00	0.70
Control delusions	0.91	0.97	0.87	2.76	1.04	3.17	4.69[a]	0.20	0.62
Guilty delusions	2.86[a]	1.77	0.41	5.11[a]	2.68	0.80	0.70	2.83	1.48
Grandiose delusions	0.66	0.97	0.14[a]	0.41	1.05	1.87	0.97	0.37[a]	0.86
Hallucinations	0.80	1.02	0.51	0.46	0.86	…	3.30	0.57	0.74
Catatonia	2.77	1.73	8.40[a]	4.57	1.64	0.88[a]	2.41	0.82	1.61
Affective flattening	0.87	1.23	5.66[a]	3.89	1.98	1.47	1.20	1.57	1.00
Affect inappropriate	0.35	0.65	0.79[a]	0.90	0.74	1.15	0.41	0.90	4.54[a]
Incoherence	0.36	0.92	0.81[a]	0.91[a]	1.64	0.88[a]	…	1.00	1.61
Loss of association	0.15	0.38	0.60	0.90[a]	0.74	1.15	1.00	0.11[a]	0.63

*All diagnoses are operationalized by DSM-III-R criteria ignoring hierarchy rules. OCD = obsessive-compulsive disorder.
[a]OR significant at .05 level, two-tailed test.

differences, apart from those found using a broader definition of schizophrenia spectrum, were found between subjects with comorbidity and those without.

Mood Spectrum Disorders With Psychotic Features

Within the group of mood spectrum psychoses, delusions of guilt, as well as catatonia and affective flattening, were more frequent among subjects with psychiatric comorbidity than those without. Conversely, incoherence and loss of association were significantly more frequent among mood spectrum psychotics without comorbidity than those with (see Table 2). As shown in Table 3, SANS total and subscale scores were higher in patients with psychiatric comorbidity than in those without. Conversely, the BPRS and the SCL-90 total scores showed only minor differences between the two groups.

To identify the specific role of each DSM-III-R Axis I diagnosis as determinant of the SCL-90, BPRS, and SANS scores, multiple regression models were performed separately in the entire cohort with, respectively, the SCL-90 total score, the nine SCL-90 subscales, the BPRS total score, the five BPRS subscales, the SANS total score, and the five SANS subscales as the dependent variables and individual psychiatric diagnoses without hierarchy as independent variables. Age and sex were also entered into the models as independent variables to adjust for their effect. Social phobia (unstandardized regression coefficient [B] = 26.06, SE = 7.68, $p < .01$) and panic disorder (B = 29.17, SE = 13.7, $p < .01$) were found to be significantly predictive of a higher SCL-90 total score.

Unipolar psychotic depression significantly predicted the BPRS total score (B = 2.83, SE = 1.34, $p < .05$), while the diagnosis of schizophrenia was found to be significantly predictive of the SANS total score (B = 14.03, SE = 4.09, $p < .001$).

As shown in Table 4, bivariate associations between specific comorbid diagnoses and each of the 12 psychotic symptoms examined were calculated separately by crude odds ratios. Odds ratios showed that social phobia comorbidity was significantly associated with somatic delusions, catatonia, and affective flattening; panic disorder with delusions of guilt; and substance abuse with somatic and control delusions.

Multiple logistic regression analyses were also performed separately using presence or absence of each of the 12 psychotic symptoms as the dependent variable after controlling for age, sex, and psychotic diagnoses. To enhance the statistical power, psychiatric comorbidity was collapsed into three categories: anxiety disorders, substance abuse disorders, and other disorders. Index episode psychotic diagnosis, age, and gender were also entered into the models to control for their potential effect. The significant associations (crude odds ratios) reported in Table 4 were confirmed. Grandiose delusions were not found to be associated with a diagnosis of bipolar disorder but with the absence of anxiety disorder comorbidity ($p < .05$).

DISCUSSION

Our findings suggest that co-occurrence of DSM-III-R Axis I psychiatric disorders is a relevant phenomenon in patients with psychotic disorders, being present in over 56% of the entire cohort. To our knowledge, the only study that systematically explored comorbidity in a cohort of psychotic inpatients is that of Strakowski et al.,[8] in which overall prevalence of Axis I psychiatric comorbidity was 40.2%, substance abuse 22.5%, obsessive-compulsive disorder 7.8%, simple/social phobia 6.9%, panic disorder 5.9%, and bulimia 4.9%. These prevalence rates are lower than those found in our study. This is likely to be due to the different characteristics of the two samples: the sample of Strakowski et al. comprised first-hospitalized patients who differed from our subjects in gender and race distribution, educational level, and physical health status and had a later mean age at onset of psy-

chosis. Conversely, prevalence rates of psychiatric comorbidity considerably higher than those of our study were found in a sample of subjects with nonaffective psychoses ascertained from the general population,[7] where only 7% of subjects with nonaffective psychosis did not receive at least one additional psychiatric diagnosis. In particular, alcohol dependence was found in 43.2% of subjects, drug dependence in 37.7%, social phobia in 39.5%, simple phobia in 30.8%, and panic disorder in 25.5%. Several factors may explain such higher level of comorbidity in the National Comorbidity Survey study. First, in Kendler and associates' study,[7] nonaffective psychoses were assessed using a different diagnostic procedure. Second, it is plausible that nonaffective psychoses ascertained from the general population were more likely to include untreated forms of illness in which affective disorder comorbidity (73.4%) was much more pronounced than in our hospitalized patients. Third, while we assessed obsessive-compulsive disorder, the overall comorbidity rate results are not directly comparable with those of the Kendler et al. study since we did not assess generalized anxiety disorder. As to the considerably higher rates of alcohol and substance abuse in the Kendler et al. study, a role was probably played by the fact that patients with alcohol dependence or substance abuse were scarcely represented in our center, because in our country these patients are usually referred to other specialized centers.

It is noteworthy that, within our nonaffective psychosis group, panic disorder comorbidity was more associated with delusional disorder and schizoaffective disorder than with schizophrenia. This can be related to the small sample size of our sample. However, an alternative explanation is that deficits of insight in schizophrenia are more severe and likely to compromise recall of a transient condition such as panic disorder, compared with the other two groups of psychotics. This should be taken into account by the clinician when assessing panic attacks in schizophrenic patients, as their recognition may have important clinical implications.[12]

In our study, multiple regression analysis showed that negative symptoms were strongly associated with a diagnosis of schizophrenia; however, when negative symptoms were assessed in mood spectrum psychoses, they were much more severe in subjects with psychiatric comorbidity than in those without. These data should be cautiously interpreted as negative symptoms have been assessed cross-sectionally without taking into account their cause, stability, or duration.[27,28] Nevertheless, they suggest that bipolar and unipolar psychotics with other concomitant Axis I disorders may be more likely than those with more pure forms of the affective illness to show schizophrenia-related features. When we investigated the role of specific comorbid diagnoses, we found that phobic disorders and substance abuse showed the strongest association with the presence of delusions and negative symptoms but not hallucinations. Analogously, psychiatric comorbidity was associated with a more severe self-reported psychopathology either in nonaffective and, though to a lesser extent, in mood spectrum psychoses. Such an association was mainly accounted for by the triad consisting of panic disorder, obsessive-compulsive disorder, and social phobia comorbidity, while substance abuse comorbidity seemed to deaden patients' expression of psychopathology. Overall, these data indicate that there is a considerable proportion of patients whose schizophrenic or mood spectrum psychosis is strictly connected with other co-occurring psychiatric disorders, which in turn have a differential weight on affecting phenomenology of psychosis. Causes of such a high rate of comorbidity and associations need to be further investigated and clarified. It is plausible that either biological and environmental causes, effect of one disorder on the subsequent onset of another disorder, and uncertainty in defining diagnostic boundaries probably all play a role to some extent.[29] However, efforts should be devoted to try to detect comorbidity profiles in larger samples of psychotic patients as one or more of these profiles might prove to be useful in advancing our understanding of the pathophysiology of psychoses and in improving our ability to offer effective treatment for psychoses.[30] Along parallel lines, our data give emphasis to the necessity of further research to clarify whether psychotic patients with different combinations of comorbid psychiatric disorders are distinct from those with "pure" forms of psychotic illness in terms of risk factors, family psychiatric history, and age at onset.

When we investigated the relationship between earlier age at first hospitalization and comorbidity, we found a positive association only in psychotic unipolar depressives but not in the other groups of psychotics. Moreover, we did not find an association between comorbidity and number of hospitalizations. Although these data are consistent with recent findings showing a lack of association between comorbidity and age at onset of schizophrenia or bipolar disorder,[31] an explanation can be found in the limited power of this study to detect such an association. On the other hand, our preliminary analyses conducted on a larger cohort of psychotic patients confirmed the lack of association (unpublished data). Therefore, it is possible that mean duration of illness in our sample (10.2 years for schizophrenia spectrum, 11.4 years for bipolar disorder, and 7.2 years for unipolar depression) was not extended enough to find such a correlation.

Finally, we found that awareness of illness did not significantly vary across the psychotic diagnostic subgroups, while it was more severe in subjects without comorbidity than in those with comorbidity, independent of their psychotic diagnosis. The relationship between insight and comorbidity may be somehow tautological, as subjects with a better insight may simply have a better ex-

pression of their psychopathology. However, we also found that specific comorbid disorders are likely to play a different role from each other on patients' self-expression of psychopathology. Such findings should contribute to stimulate research on the reciprocal relationships between level of insight structure, patient's own construction of experience, and effects exerted by concomitant formation and development of multiple disorders in the same individual.[32–34]

It is important to acknowledge several limitations of this study. First, we studied only hospitalized patients, limiting the applicability of these results to patients with psychotic disorders in general. The fact that our center specializes in the treatment of anxiety and mood disorders might have contributed to a selection bias, with an overrepresentation of mood disorders to the detriment of nonaffective psychoses. Rates of lifetime comorbidity and psychopathology could have been distorted by patients' or relatives' recall bias, particularly in schizophrenia spectrum disorders, which may have had an insidious onset. Analyses were performed independently of whether psychotic patients were at their first or subsequent psychotic episode. Analyses of bipolar psychotics were carried out without discriminating between those with prevalent manic episodes and those with predominantly depressive episodes, which may differ from each other on several phenomenological characteristics.

The main objective of investigating comorbidity is to help refine definitions of syndromes and diagnoses.[35,36] Psychiatric comorbidity in psychosis may be overshadowed by prominent psychotic disturbances or trivialized by clinicians when their intervention imposes the identification and treatment of most severe symptoms such as delusions, hallucinations, or behavioral abnormalities. However, an increasing number of studies and clinical reports show that the assessment of psychiatric comorbidity provides clinicians and researchers with a useful clinical construct to capture additional components of the heterogeneous phenomenology of psychoses, an approach that may have substantial therapeutic implications.[30,37–39]

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