Neurocognitive Impairment in Bipolar Patients With and Without History of Psychosis

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Objective: Little is known regarding the impact of psychotic symptoms on the cognitive functioning of bipolar patients. Findings from previous reports are controversial and mainly focused on current psychotic symptoms. The main aim of this study was to ascertain whether the history of psychotic symptoms was associated with greater cognitive impairment in euthymic bipolar patients.

Method: Sixty-five euthymic bipolar disorder patients (DSM-IV criteria; 35 with a history of psychotic symptoms and 30 without such a history) were assessed through a neuropsychological battery targeting attention, psychomotor speed, verbal memory, and executive functions. Thirty-five healthy controls were also included in the study in order to compare the neuropsychological performance among groups. Multivariate analysis of covariance was performed controlling for the effect of residual depressive symptoms as a covariate. The study was conducted from June 2005 to June 2006.

Results: Bipolar patients with a history of psychotic symptoms showed a higher number of manic episodes and more hospitalizations than patients without such a history (both $p < .001$). Regarding neuropsychological performance, patients with a history of psychotic symptoms performed more poorly than those without such a history or controls in all verbal memory measures ($p < .005$). Furthermore, patients with a history of psychotic symptoms were more impaired on tasks related to executive functions compared to healthy controls ($p < .05$). History of psychotic symptoms was found to be a predictor of verbal memory impairment.

Conclusions: Our findings suggest that the history of psychotic symptoms may partly account for the cognitive dysfunctions seen in euthymic bipolar patients, especially with regard to persistent verbal memory dysfunction, as well as with some executive dysfunctions.

(J Clin Psychiatry 2008;69:233–239)

Received Nov. 15, 2006; accepted May 29, 2007. From the Department of Psychiatry, Bipolar Disorder Program, Clinical Institute of Neuroscience, Hospital Clinic of Barcelona, August Pi i Sunyer Institute of Biomedical Research (IDIBAPS), University of Barcelona, Barcelona, Spain, and the Stanley Medical Research Institute, Bethesda, Md. (Drs. Martinez-Aran, Torrent, Salamero, Daban, Sanchez-Moreno, Goikolea, Benabarre, Colom, and Vieta); and the Teaching Unit of Psychiatry and Psychological Medicine, Department of Medicine, University of Valencia, Valencia, Spain (Drs. Tabares-Seisdedos and Balanza-Martinez).

This study was supported by grants from the Spanish Ministry of Health, Instituto de Salud Carlos III (FIS: PI050206; PI051293) and RETICS RD06/0011 (REM-TAP Network), and the Stanley Medical Research Institute (Bethesda, Md.).

The authors thank Jan Scott, Ph.D., F.R.C.Psych., University of Newcastle, Newcastle upon Tyne, and Institute of Psychiatry, London, England, for her valuable comments on the reviewed manuscript. Dr. Scott reports no financial or other relationships relevant to the subject of this article.

Dr. Sanchez-Moreno is a member of the speakers/advisory boards for Faes Pharma. Dr. Benabarre is a consultant for Pfizer and is a member of the speakers/advisory boards for Pfizer, Eli Lilly, and Janssen. Dr. Colom has received honoraria from Sanofi, AstraZeneca, Eli Lilly, and Tecnifar, and is a member of the speakers/advisory board for Shire. The other authors declare no conflicts of interest relevant to the content of this article.

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There is increasing evidence of persistent dysfunctions in bipolar patients with regard to several cognitive areas, such as verbal memory, executive functions, or attention.[1–6] The literature suggests a relationship between cognitive impairment and several clinical variables, such as residual affective symptoms, number and subtype of episodes, duration of illness, age at illness onset, and number of admissions.[2,3,6,7] Nevertheless, there are other potential clinical factors associated with a poorer illness outcome, such as rapid cycling, history of substance abuse or dependence, or history of psychotic symptoms, that have not been systematically investigated. Research on the impact of psychotic symptoms on cognition in bipolar disorder is scarce and controversial. Only a few studies have been conducted on bipolar patients with and without current psychotic symptoms. In these, bipolar patients were compared with schizophrenia patients, generally, in an acute phase of the illness. Most of the studies did not

control for the effect of psychotic symptoms on cognition in bipolar patients. Albus et al.[8] compared first-episode affective disorder and schizophrenia patients with and without psychotic symptoms. These authors suggested that the impact of psychotic symptoms on cognition was more important than diagnosis, as patients with psychotic symptoms performed worse on cognitive measures than patients without psychotic symptoms, independent of diagnosis. Although several authors[9,10] have failed to find differences in neuropsychological performance between bipolar patients with and without current psychotic symptoms, Zubieta et al.[11] found poorer performance in attention, verbal learning, and executive functions in bipolar patients with a history of psychotic symptoms compared to healthy controls. In addition, Martinez-Aran et al.[2,3] observed that bipolar patients with a history of psychotic symptoms were more impaired in verbal memory tasks than patients without such a history. More recently, Glahn et al.[12] found that spatial working memory performance clearly distinguished bipolar patients with and without history of psychotic symptoms. In contrast, 3 previous studies did not find differences in neurocognitive performance between euthymic bipolar patients with a history of psychosis and bipolar patients without such a history.[13–15]

To our knowledge, there is no published research using restrictive remission criteria that focuses specifically on the impact of history of psychotic symptoms on the cognitive functioning of euthymic bipolar patients. Moreover, the history of psychotic symptoms was assessed in patients who were recruited and followed prospectively in our program. Our main hypothesis was that the history of psychotic symptoms would negatively influence verbal memory and executive functions in euthymic bipolar patients.

METHOD

With the approval of the hospital ethical committee, study participants were enrolled from the Bipolar Disorders Program of the Hospital Clinic of Barcelona. All patients met DSM-IV criteria for bipolar I or II disorder and were euthymic. The clinical state of the patients was determined by a psychiatrist responsible for the follow-up at the Bipolar Disorders Program using DSM-IV criteria and the Structured Clinical Interview for DSM-IV (SCID)[16] and the Spanish versions of the 17-item Hamilton Rating Scale for Depression (HAM-D-17)[17,18] and the Young Mania Rating Scale (YMRS).[19,20] Euthymia was defined as YMRS score ≤ 6 and HAM-D-17 score ≤ 8 during monthly visits over a 6-month period. The history of psychotic symptoms was well documented and was defined as the occurrence of delusions and/or hallucinations during at least 1 affective episode, using DSM-IV criteria. This definition was consistent with previous studies.[12,21,22] Twenty-two patients had a history of mood-congruent delusions, 17 had a history of mood-incongruent delusions, and 4 had both. Eight patients had a history of visual hallucinations, 15 had a history of auditory hallucinations, and 5 had both. Nineteen patients had a history of both delusions and hallucinations, while 16 reported only delusions. Absence of psychotic symptoms for the 6 months prior to testing was verified at the monthly consecutive visits with the psychiatrist. No subjects had a history of psychosis in the absence of affective symptoms and none met criteria for schizoaffective bipolar disorder.

After screening for inclusion, 35 bipolar patients with a history of psychotic symptoms and 30 bipolar patients without a history of psychotic symptoms were included along with 35 healthy controls. The exclusion criteria were history of head injury or loss of consciousness, neurologic illness, substance dependence in the last year, mental retardation (IQ < 70), significant medical illness, electroconvulsive therapy in the last year, and affective or mood fluctuations in the last 6 months. Of 90 potential participants, 22 met 1 or more exclusion criteria. The most common reason for exclusion (N = 18) was the presence of persistent subsyndromal symptoms during the prior 6 months. Sixty-five of the 68 bipolar patients who met criteria for euthymia gave written informed consent to participate in the study after procedures had been fully explained. Ninety-six percent of patients were maintained on their medications during the 4 weeks before neuropsychological testing.

Thirty-five healthy comparison subjects without psychiatric or neurologic history were also recruited via advertisement and from a known pool of normal volunteers. Controls were screened for Axis I psychiatric disorders using the SCID,[16] and none had first-degree relatives with bipolar disorder. Six subjects had to be excluded (2 due to history of head injury and 4 due to anxiety disorders). The study was conducted from June 2005 to June 2006.

Clinical and Psychosocial Assessment

Clinical and psychosocial data were collected routinely as part of the clinical protocol at the Bipolar Disorders Program. Clinical status of bipolar patients was established using the SCID, the YMRS, and the HAM-D-17, while functioning status was assessed using the Social and Occupational Functioning Assessment Scale (SOFAS).[23]

Neuropsychological Assessment

The neuropsychological evaluation was carried out by a trained neuropsychologist who was blind to the results of the clinical and psychosocial assessments.

An extensive review of previous literature on this issue guided the choice of neuropsychological tests used in the present study. In order to enhance replication, only tests frequently documented by the neuropsychological literature were employed.[24,25]

Premorbid IQ was estimated using the vocabulary subtest of the Wechsler Adult Intelligence Scale (WAIS).[26] Frontal executive functions were evaluated with the Wisconsin Card Sorting Test (WCST),[27] Stroop Color-Word Interference Test,[28] and Controlled Oral Word Association Test (FAS and Animal Naming subtests).[29]

Attention/concentration and mental tracking were assessed with the digit subtest (digits forward and backward from the WAIS)[26] and the Trail Making Test, parts A and B (TMT-A and TMT-B).[30] Verbal learning and memory were evaluated with the California Verbal Learning Test (CVLT).[31]

Statistical Analyses

Data analyses were performed using SPSS, version 12.0 (SPSS Inc., Chicago, Ill.). Comparison of clinical and sociodemographic characteristics across groups (bipolar patients with a history of psychotic symptoms, bipolar patients without a history of psychotic symptoms, and healthy controls) was carried out using analysis of variance (ANOVA) and χ^2 tests. Performance on the neuropsychological tests was compared across the 3 groups by means of ANOVA. Since multiple dependent variables were used, a prior protective multivariate analysis of covariance was performed with residual depressive symptoms according to the HAM-D-17 score as a covariate and group as a main factor. Since neuropsychological tests are naturally correlated, this procedure was considered superior to a Bonferroni inequality correction as the latter would increase type II errors. Group differences were tested in one-way ANOVA, followed by Tukey's post hoc comparison procedure when significant main effects were present. Effect sizes (Cohen's d) were also calculated.

The potential impact of clinical variables such as diagnostic subtype (bipolar I or II), number of manic episodes, and medication (lithium and antipsychotics) were controlled for in the analysis of differences in the cognitive performance between the 2 patient groups. First, an ANOVA was performed, and after that, we controlled for the effect of each confounder on cognition using multivariate analyses of variance. Since verbal memory was significantly more impaired in bipolar patients with a history of psychotic symptoms, we tried to establish which factors would predict verbal memory dysfunction using hierarchical linear regression models. Following previous reports and examination of our own empirical data, clinical and pharmacologic variables were included in the models using a stepwise method.

RESULTS

The clinical and demographic characteristics of the 3 groups are shown in Table 1. No differences between groups were found with respect to age, sex, years of education, or estimated premorbid IQ.

The patient groups differed from one another in the number of previous manic and hypomanic episodes as well as the number of hospitalizations. More manic episodes and admissions were observed in the group with a history of psychosis, whereas more hypomanic episodes were found in the group without such a history (Table 1). Moreover, significant differences were found with respect to bipolar subtype. Another interesting finding was that bipolar patients with a history of psychosis showed poorer psychosocial functioning as measured through the SOFAS compared to patients with no history of psychosis. Significantly more patients with a history of psychosis were unemployed.

With regard to neuropsychological performance, even after controlling for the effect of mild subdepressive symptoms, the group with a history of psychotic symptoms was more impaired on verbal memory and frontal executive function tests. As shown in Table 2, bipolar patients with a history of psychotic symptoms showed a significantly poorer performance on all CVLT measures (except Recognition) compared to bipolar patients without a history of psychotic symptoms, with effect sizes in the moderate range, and compared to healthy controls, with larger effect sizes. The group with a history of psychotic symptoms also significantly differed from controls on executive function measures, such as the WCST, especially with respect to the number of total errors, perseverative errors, and perseverative responses, as well as on other measures assessing semantic fluency (Animal Naming). Other neuropsychological measures more specifically related to working memory, such as digits backward and TMT-B, were also more impaired in the group with a history of psychotic symptoms than in the control group. On attention and psychomotor speed tasks (digits forward and backward and TMT-A), both patient groups showed a similar performance. Small effect sizes were obtained for differences in WCST performance between patients with and without a history of psychotic symptoms.

We also tried to identify differences between patients with and without a history of psychotic symptoms on cognitive performance, controlling separately for the effect of the potential confounders identified in Table 1. As there were more bipolar I patients in the group with a history of psychosis and more bipolar II patients in the group without such a history, diagnostic subtype was controlled for statistically by using multivariate ANOVA. Bipolar subtype seemed to have a limited influence on frontal executive measures, such as WCST total errors ($F = 2.56$, $p = .085$), TMT-B ($F = 2.94$, $p = .061$), and Animal Naming ($F = 2.32$, $p = .107$), but did not significantly influence the other neuropsychological variables. The number of previous manic episodes, when controlled for, did not influence results.

Regarding medication, more patients with a history of psychotic symptoms were treated with lithium and

Table 1. Demographic, Clinical, and Pharmacologic Variables of Bipolar Disorder Patients and Controls

Variable	Patients With History of Psychosis (N = 35) Mean	SD	Patients Without History of Psychosis (N = 30) Mean	SD	Control Group (N = 35) Mean	SD	Statistic[a] F	df	p Value
Age, y	39.9	8.9	42.1	9.7	39.1	12.1	0.70	2,99	.49
Educational level, y	12.3	3.6	14.2	2.9	12.9	3.3	2.41	2,98	.09
Estimated premorbid IQ	110.3	6.9	112.9	8.0	113.9	9.2	1.90	2,99	.15
Age at onset, y	25.6	7.7	27.3	10.0	…	…	0.57	1,61	.45
Chronicity	15.1	7.3	13.5	8.5	…	…	0.60	1,58	.44
Total episodes	11.4	10.5	12.0	10.8	…	…	3.95	1,60	.051
Manic episodes	3.2	3.5	0.5	1.0	…	…	13.94	1,58	< .001
Hypomanic episodes	1.6	2.0	7.0	7.1	…	…	17.47	1,58	< .001
Depressed episodes	4.2	2.9	7.3	6.7	…	…	5.91	1,60	.018
Mixed episodes	0.6	0.9	0.9	2.5	…	…	0.64	1,57	.43
Hospitalizations	3.0	2.6	0.4	0.9	…	…	28.08	1,62	< .001
Suicide attempts	0.7	1.3	0.7	1.3	…	…	0.002	1,59	.97
HAM-D-17 score	4.1	2.7	2.3	2.4	1.8	1.3	10.39	2,99	< .001
YMRS score	1.2	1.6	1.3	1.9	0.8	0.9	0.83	2,99	.44
SOFAS score	62.9	14.5	70.6	14.5	…	…	4.61	1,64	.036
	N	%	N	%	N	%	χ^2	df	p Value
Sex									
Male	12	34.3	15	50.0	13	37.1	1.84	2,1	.39
Female	23	65.7	15	50.0	22	62.9			
Unemployed[b]	26	74.3	13	44.8	…	…	5.78	1,64	.022
Bipolar type I	30	85.7	7	23.3	…	…	25.6	1,65	< .001
Family history of affective disorder[b]	17	54.8	16	57.1	…	…	0.03	1,59	1.0
Medications[b]									
Lithium	27	79.4	15	51.7	…	…	5.40	1,63	.031
Carbamazepine	8	23.5	1	3.6	…	…	4.93	1,62	.033
Valproate	1	2.9	5	17.9	…	…	5.34	1,62	.069
Antidepressants	9	25.7	12	42.9	…	…	2.06	1,63	.185
Antipsychotics	19	54.3	6	20.3	…	…	7.52	1,64	.010

[a]F statistics determined by ANOVA; χ^2 statistics determined by χ^2 tests.
[b]A few patients had missing data for this variable.
Abbreviations: ANOVA = analysis of variance, HAM-D-17 = 17-item Hamilton Rating Scale for Depression, SOFAS = Social and Occupational Functioning Assessment Scale, YMRS = Young Mania Rating Scale.
Symbol: … = not applicable.

antipsychotics compared to patients without a history of psychotic symptoms; therefore, the potential effect of these medications was also statistically controlled for. Lithium treatment was almost significantly associated with WCST total errors (F = 2.97, p = .09) and other executive function measures, such as TMT-B (F = 2.64, p = .11) and Animal Naming (F = 3.42, p = .07). After controlling for the effect of antipsychotic medication, differences between patient groups changed to be statistically significant on WCST perseverative errors (F = 4.08, p = .048), perseverative responses (F = 4.45, p = .039), and TMT-A (F = 4.46, p = .039), but differences between groups on semantic verbal fluency disappeared (F = 2.96, p = .09). Antipsychotic medication did not seem to influence the other neuropsychological measures. With respect to the effect of the confounders, in these tests the change in p values was marginal.

Since verbal memory was the cognitive domain that was more impaired in the group with a history of psychotic symptoms as compared to nonpsychotic patients and healthy subjects, we used hierarchical regression models to identify predictors of verbal memory impairment as measured through the CVLT (learning list, short-delay free recall, and long-delay free recall). The regression analyses were computed for the whole bipolar group. Following findings of previous reports,[3,32] and our own empirical findings, the clinical and pharmacologic variables introduced in the 3 models (for the 3 CVLT measures) were history of psychotic symptoms, HAM-D-17 scores, use of antipsychotics and lithium, number of hospitalizations, and manic episodes. These variables were entered using a stepwise method. Linear regression analyses showed that the history of psychotic symptoms was the variable that best predicted verbal memory dysfunctions, after which, the other variables did not enter in the equation. Performance on the verbal learning task was associated with the presence of psychotic symptoms in the past (t = 3.49; df = 1,55; β = 0.425; p = .001) with an adjusted R^2 = 0.166. Performance on immediate free recall was also associated with a history of psychotic symptoms (t = 3.37; df = 1,55; β = 0.414; p = .003). History of psychotic symptoms accounted for 15.6% of the variance. Finally, history of psychotic symptoms was also a good predictor of poor delayed free recall (t = 2.71;

Table 2. Neuropsychological Performance in Bipolar Patients With and Without History of Psychotic Symptoms

	Patients With History of Psychosis		Patients Without History of Psychosis		Control Group		MANCOVA		Tukey Post	Cohen's d		
Measure	Mean	SD	Mean	SD	Mean	SD	F (df = 2,97)	p Value	Hoc Test[a]	A vs B	B vs C	A vs C
Frontal executive function												
WCST												
Total errors	32.3	23.3	22.1	14.1	20.3	14.7	4.70	.011	A < C	0.52	0.12	0.61
Perseverative responses	21.2	20.8	13.4	14.1	9.5	8.2	6.0	.004	A < C	0.43	0.33	0.74
Perseverative errors	17.7	15.5	12.3	11.9	8.7	6.8	5.80	.004	A < C	0.39	0.34	0.75
SCWT-Interference	2.1	5.3	0.9	7.9	4.7	7.0	2.56	.08	…	0.17	0.50	0.41
Attention/concentration and mental tracking												
Digit subtest (from WAIS)												
Digits forward	5.6	0.9	5.7	1.5	6.5	1.3	5.30	.007	A = B < C	0.08	0.56	0.80
Digits backward	4.2	0.9	4.2	1.0	5.0	1.2	5.35	.006	A = B < C	0	0.72	0.75
TMT												
Trail A	43.9	17.6	37.7	12.4	30.2	11.6	6.70	.002	A < C	0.40	0.62	0.91
Trail B	107.5	56.8	81.5	30.9	74.6	37.1	4.29	.017	A < C	0.56	0.20	0.68
Verbal fluency												
FAS	34.5	9.5	35.9	11.4	39.6	11.9	3.49	.035	…	0.13	0.31	0.47
Animal Naming	17.5	3.7	19.7	4.5	22.1	6.1	6.09	.003	A < C	0.53	0.44	0.91
Verbal learning and memory												
CVLT												
List A (total)	42.4	10.7	49.9	12.2	53.5	9.6	6.85	.002	A < B = C	0.65	0.32	1.09
Short-delay free recall	8.7	3.4	11.2	3.1	11.3	3.3	7.77	.001	A < B = C	0.76	0.03	0.77
Short-delay cued recall	10.2	2.7	11.9	2.5	12.7	2.3	8.57	< .001	A < B = C	0.65	0.33	0.99
Long-delay free recall	9.5	3.1	11.4	3.3	12.5	3.0	8.49	< .001	A < B = C	0.59	0.34	0.98
Long-delay cued recall	10.0	3.0	12.1	2.6	13.0	2.6	10.11	< .001	A < B = C	0.74	0.34	1.06
Recognition	13.6	2.1	14.3	1.9	15.0	1.3	2.99	.055	…	0.34	0.43	0.80

[a]A = patients with history of psychosis, B = patients without history of psychosis, C = control group.
Abbreviations: CVLT = California Verbal Learning Test, MANCOVA = multivariate analysis of covariance, SCWT = Stroop Color-Word Interference Test, TMT = Trail Making Test, WAIS = Wechsler Adult Intelligence Scale, WCST = Wisconsin Card Sorting Test.
Symbol: … = not significant.

df = 1,55; $\beta = 0.343$; p = .009), explaining 10.2% of the variance.

DISCUSSION

Our findings suggest that euthymic bipolar patients with a history of psychotic symptoms are cognitively more impaired than healthy subjects. On specific areas, such as verbal memory, they are even more impaired than patients without such a history as suggested previously by other authors.[2,3,11,33] The group with a history of psychosis had lower total learning scores on the CVLT than did the group without such a history. These findings suggest that patients with a history of psychotic symptoms show difficulties mainly in the encoding or acquisition of new information; as less information is learned, less is recalled. However, the actual cognitive impairment is not that simple. Probably, as Robinson and Ferrier[32] suggested, there is an overlap between verbal memory and executive function domains using tests such as the CVLT, so that the encoding process involves frontal executive functions for the use of semantic strategies to encode information. Although cognitive impairment seems to be more associated with history of psychotic symptoms, patients who never experienced psychotic symptoms also showed difficulties on several cognitive measures, showing medium effect sizes for such measures as attention/working memory and psychomotor speed (digits forward and backward and TMT-A).

Recently, Glahn et al.[12] found that lifetime history of psychosis in bipolar patients may have a negative impact on spatial working memory. Moreover, independent of diagnosis, patients with schizophrenia or bipolar disorder with a positive family history of psychotic illness exhibited a significantly worse performance on tests of visual-motor processing and selective attention than did those without such a history.[34] However, Selva et al.[10] did not find differences on cognitive performance between bipolar patients with and without a history of psychotic symptoms. Both bipolar groups were more impaired than the normal controls in attention, verbal memory, verbal fluency, and executive functions, except for difficulties in completing the Stroop test that were greater in patients with a history of psychotic symptoms. The authors suggested that euthymic patients should be assessed to evaluate the impact of psychotic symptoms on cognition.[10] However, lack of statistical power might explain the failure to find differences between groups. The absence of differences on cognitive performance between bipolar patients with and without a history of psychotic symptoms

may indicate that cognitive impairments are associated with the bipolar illness itself, independently of psychotic symptoms.

The present findings on euthymic patients suggest that, in general, bipolar patients are cognitively more impaired than healthy subjects, but those patients with psychotic symptoms in the past are more likely to show cognitive dysfunction and, probably, to have a similar performance to schizophrenic patients than patients without psychotic symptoms.[8,12] Glahn et al.[12] have suggested that bipolar disorder with psychotic features may represent a distinct subgroup of bipolar disorder with working memory impairments that are quantitatively and qualitatively similar to those of patients with schizophrenia and schizoaffective disorder. In this regard, Evans et al.[35] reported poorer cognitive performance in patients with schizophrenia spectrum diagnoses as compared to nonpsychotic affective patients.

Several authors have indicated that antipsychotics may influence the cognitive functioning of patients rather than psychotic symptoms themselves.[13,14] In our sample, more patients with a history of psychotic symptoms were taking antipsychotics compared to the group without such a history. When controlled for in the analysis, antipsychotics had limited influence on some frontal executive function measures. When we controlled for the effect of lithium, which was more commonly used in bipolar patients with a history of psychotic symptoms, results also differed with respect to several executive function measures, but not verbal memory performance. Previous studies reported that antipsychotics may have a more deleterious effect on cognition than lithium,[13,36] but our findings suggest that lithium and antipsychotics may slightly influence some executive function measures. Recent publications have also reported persistent executive dysfunctions in euthymic bipolar patients treated with lithium.[37] Therefore, differences between groups in the performance on executive tasks could be modulated, in part, by pharmacologic factors. In any case, the change in p values on these cognitive measures was marginal. With respect to other medications, only 2 patients were taking anticholinergic drugs, and 13 patients were receiving benzodiazepines (8 with a history of psychotic symptoms and 5 without such a history). No patient was treated with stimulants.

Differences in diagnosis subtype may lead to the conclusion that bipolar I patients, who more frequently had a history of psychosis, are more likely to show cognitive dysfunction. After we controlled for the effect of diagnosis subtype, differences between groups on some measures of executive function (WCST total errors, TMT-B, Animal Naming) were no longer apparent. Once more, the changes in p values were marginal, indicating that differences between patients with and without a history of psychotic symptoms on neuropsychological functioning are not due to diagnostic subtype. Also, recent studies suggest that bipolar II patients may also show cognitive deficits.[38] Our findings support the hypothesis of a continuum between mood disorders and the schizophrenic spectrum, in which psychotic symptoms play an important role. These findings suggest similarities in neuropsychological performance in schizophrenic and bipolar patients,[39,40] and one might speculate that bipolar patients with past psychotic symptoms are more similar, from a neurocognitive point of view, to schizophrenic and schizoaffective patients than bipolar patients without past psychotic symptoms, especially with respect to verbal memory dysfunction. Number of hospitalizations is probably a proxy measure of illness severity, and as such, the fact that patients with a history of psychotic symptoms had more admissions and also had greater cognitive impairment may suggest that a direct relationship exists between severity and neurocognitive functioning. Number of manic episodes did not seem to influence results.

Low premorbid intellectual functioning has been found in schizophrenic but not in nonpsychotic bipolar patients.[41] These authors have suggested that a normal premorbid functioning may protect against the occurrence of psychosis. The directionality between impaired cognition and psychosis is not clear. In schizophrenic patients, cognitive impairment seems to be present before the appearance of psychotic symptoms. This may also be true for a subgroup of bipolar patients.[42] Moreover, cognitive dysfunctions may also be present in unaffected first-degree relatives of schizophrenic or bipolar patients.[43]

The best predictor of poor verbal memory functioning was the lifetime history of psychotic symptoms, especially with regard to learning or acquisition of new information. Previous reports suggested that there might be some relationship between psychotic symptoms and verbal learning, but as far as we know, this is the first study reporting the predictive value of psychotic symptoms on cognition, and particularly on verbal memory, in euthymic bipolar patients. Other putative predictors did not significantly enhance the model.

The strength of the present study is that it is the first to assess the neuropsychological performance of euthymic bipolar patients with and without lifetime history of psychotic symptoms. Moreover, a broad range of neuropsychological tests were used, whereas other previous studies focused on specific cognitive areas or did not differentiate between clinical phases. Our findings indicate the relevance of distinguishing different subgroups in bipolar disorder in order to study the impact of clinical variables, such as psychotic features, on cognitive functioning, and particularly on verbal memory.

Among limitations, the definition of psychotic symptoms only captured hallucinations and delusions, so disorganized thought or behavior were not considered; therefore, it is possible that a few cases may have been misclassified as nonpsychotic patients. Also, our sample

size did not allow us to analyze other specific features related to positive history of psychotic symptom status, such as mood-congruent versus incongruent delusions or hallucinations versus delusions.

Further research should take into account the distinction between bipolar patients with and without a history of psychotic symptoms regarding neuropsychological performance.[12,21] The study of delusions following mood-congruent and mood-incongruent criteria would be interesting in order to determine if greater impairment is associated with the latter.[10]

Drug names: carbamazepine (Carbatrol, Tegretol, and others), lithium (Eskalith, Lithobid, and others).

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