RESEARCH ARTICLE

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Neurocognitive functioning in early-onset and late-onset older patients with euthymic bipolar disorder

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Objective: Most neurocognitive studies have not taken into account the fact that older patients with bipolar disorder (BD) are a heterogeneous population. The main goal of this study was to compare neurocognitive performance and extrapyramidal symptoms in older patients with early-onset BD (EO-BD) and late-onset BD (LO-BD).

Methods: Euthymic older patients with EO-BD ($n = 20$), LO-BD ($n = 20$), and healthy controls ($n = 20$) were evaluated with traditional clinical instruments and measures of exposure to psychotropic drugs, as well as extrapyramidal symptoms. All subjects completed an extensive neuropsychological battery.

Results: Patients with EO-BD showed poorer performance than healthy controls in two measures of verbal memory and two measures of executive functions, whereas patients with LO-BD exhibited lower performance scores than healthy controls in almost all of the measures assessed. Impairments in the LO-BD group included even neurocognitive domains typically spared in mixed-age patients. Additionally, there was a trend toward displaying higher extrapyramidal symptoms in the LO-BD group compared with both EO-BD and healthy control groups. In both patient groups, psychosocial functioning was related with executive dysfunction and extrapyramidal symptoms.

Conclusions: Patients with LO-BD may have more extensive and severe cognitive impairments, as well as higher vulnerability to extrapyramidal symptoms, compared with patients with EO-BD. Cognitive–motor disturbances may help to explain impairments in daily functioning among older patients with EO-BD and LO-BD during remission.

Key words: bipolar disorder; neuropsychology; age at onset; frontotemporal dementia; cerebrovascular disease
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Introduction

The number of people with severe mental illnesses who are reaching old age will increase dramatically over the next several decades (Jeste *et al.*, 1999). Persons aged 60 years and older may constitute as much as 25% of the population with bipolar disorder (BD) (Sajatovich *et al.*, 2005). In this context, furthering our knowledge about the clinical features of BD in the older population is critical.

There is a growing body of evidence stipulating that mixed-age patients with BD have impairments in neurocognitive functioning even during euthymic periods. Independent meta-analyses have concluded that the main cognitive domains affected in remitted patients are verbal memory, attention, and executive function (Robinson *et al.*, 2006; Torres *et al.*, 2007). However, the neurocognitive functioning of older people with BD has been a largely neglected issue, which became the focus of several studies only in the last years. In fact, Young *et al.* (2006) conducted a review about neurocognition in BD in the old age and found only seven studies that have concluded that these patients could display cognitive impairments. Moreover, just two of those studies evaluated euthymic patients, and the cognitive tests used provide only an overall assessment of cognitive functioning, not particularly useful to characterize the profile of cognitive impairments (Broadhead and

Jacoby, 1990; Gildengers *et al*., 2004). Recently, several studies assessed the neurocognitive functions of older euthymic patients with BD across a range of cognitive domains (Gildengers *et al*., 2007; Schouws *et al*., 2007; Martino *et al*., 2008; Delaloye *et al*., 2009a, 2009b). These studies provide evidence that neurocognitive impairments in older BD patients are comparable in terms of both affected functions and magnitude to those previously reported in younger patients.

However, almost all neurocognitive studies did not take into account that older patients with BD actually constitute a heterogeneous population composed of both early-onset patients (EO-BD) who develop their illness during early adulthood and late-onset patients (LO-BD) who experienced their first mood episode at an older age. Different studies using admixture analysis (a method that identifies the theoretical model that best fits with the observed distribution of age at onset in an epidemiologic sample of BD patients) have recognized a late-onset subgroup of BD (Bellivier *et al*., 2001; Bellivier *et al*., 2003). The peak of age at onset found in the largest of these studies for the LO-BD group was 39.2 years (SD = 9.6), comprising 21.2% of cases (Bellivier *et al*., 2003). The distinction between older BD patients by age at onset is critical because, typically, LO-BD patients show a less frequent family history of affective disorders and higher frequency of neurological comorbidities than EO-BD patients, suggesting that there may be an influence of non-genetic etiological factors within this subgroup (Shulman and Post, 1980; Schürhoff *et al*., 2000; Moorhead and Young, 2003; Depp and Jeste, 2004). Therefore, the profile of cognitive impairments is expected to be presumably different in these subgroups of older patients. The first study that explored neurocognitive functioning between early-onset and late-onset older euthymic patients with BD using the Dementia Rating Scale failed to find any differences between the groups, thus not supporting the hypothesis of different etiologies (Depp *et al*., 2004). However, another recent study specifically designed to assess cognitive performance in these populations showed that LO-BD patients were more impaired in psychomotor performance and mental flexibility than EO-BD patients (Schouws *et al*., 2009). These scarce and inconclusive data stress the need for further neurocognitive studies to explore the neurocognitive profile of EO-BD and LO-BD patients.

From a clinical perspective, it is crucial to understand the neurocognitive functioning of these subgroups of older patients because of the impact it may have on the very real vocational and social challenges that patients have to deal with on a daily basis (Gildengers *et al*., 2007; Martino *et al*., 2008; Delaloye *et al*., 2009b); and for obvious reasons, it is crucial to understand its possible connection with different etiological mechanisms. Therefore, the main aim of this study was to explore cognitive performance in a sample of early-onset and late-onset older bipolar patients with strict euthymic criteria by using a comprehensive neurocognitive battery. Two additional aims were to compare EO-BD and LO-BD patients in terms of neurological features and to assess the influence of neurocognitive impairments and neurological features in psychosocial functioning in these subgroups of patients. On the basis of previous studies, we hypothesized that LO-BD patients would show poor performance in neurocognitive performance than EO-BD patients.

Methods

Forty subjects with BD (20 EO-BD and 20 LO-BD) were consecutively selected from the outpatient population of the Bipolar Disorder Program of the Favaloro University with the following inclusion criteria: age older than 60 years old, diagnosis of BDI or BDII according to DSM-IV using Structured Clinical Interview for DSM-IV (SCID) (First *et al*., 1996), and euthymic [defined by Hamilton Depression Rating Scale (HDRS) ≤8 and Young Mania Rating Scale (YMRS) ≤6] for at least 8 weeks. Definition of "age at onset" was establish as the age at which the patient first met DSM-IV criteria for major depressive episode, mixed episode, mania, or hypomania according to clinical charts and interviews. On the basis of previous epidemiological (Bellivier *et al*., 2003) and neurocognitive studies (Depp *et al*., 2004; Schouws *et al*., 2009), we defined early-onset and late-onset of illness as a first affective episode in patients below and over 40 years of age, respectively. Exclusion criteria included a history of alcohol dependence or substance abuse, history of mental retardation, neurological disease, or any unstable clinical condition (such as hypothyroidism or diabetes) that could affect cognitive performance. We also excluded patients that received electroconvulsive therapy in the last 2 years and patients with a clinical diagnosis of dementia. Additionally, 20 healthy controls matched by age and years of education were included. These participants had neither a history of neurological disease nor a history of psychotic or affective disorders among themselves or first-degree family members, and they were not taking psychotropic medication. The study was approved by the Hospital Ethics Committee in accordance

with the Helsinki Declaration of 1975. All subjects gave written informed consent for their participation after receiving a complete description of the study.

Clinical assessment

In addition to SCID, all subjects were evaluated with the HDRS (Hamilton, 1960), the YMRS (Young *et al.*, 1978), and the Unified Parkinson's Disease Rating Scale (UPDRS)-III Section (van Hilten *et al.*, 1994) to assess extrapyramidal symptoms. Psychosocial functioning was assessed with the General Assessment of Functioning (GAF) (DSM-IV). The rater was instructed to use the GAF to measure functioning — and not symptoms — during the last month, because other measures of mood symptoms (HDRS and YMRS) were obtained as part of the study. Additional clinical information was obtained from medical case notes and direct patients' interviews. Exposure to antidepressants, mood stabilizers, antipsychotics, and benzodiazepines was assessed with the Clinical Scale of Intensity, Frequency, and Duration of Psychopharmacological Treatment (IFD) (Peralta and Cuesta, 2002). This scale provides a quantitative measure of current exposure to different groups of psychotropic medications on a 0–5 point range (0 = no medication, 1 = sporadic low dose, 2 = continue low dose; 3 = middle dose, 4 = high dose, and 5 = very high dose).

Neurocognitive assessment

Patients and healthy controls completed a neurocognitive battery designed to assess the following: (i) attention: Forward Digit Span (Wechsler, 1955); (ii) verbal memory: Memory Battery of Signoret (Signoret and Whiteley, 1979) — this test assesses immediate and delayed recall of a short story — and the serial learning of a 12-word list of different semantic categories (three trials), free delayed recall, and recognition with semantic clues and multiple options; (iii) language: Boston Naming Test (Kaplan *et al.*, 1983); and (iv) executive functions: Wisconsin Card Sorting Test (WCST) (Heaton, 1981), verbal fluency (Benton *et al.*, 1983), and Backward Digit Span (Wechsler, 1955). Neuropsychological tests were grouped in these domains on the basis of previous literature in BD (Martinez-Arán *et al.*, 2004; Robinson *et al.*, 2006; Torres *et al.*, 2007). Additionally, estimated premorbid intelligence quotient (IQ) was calculated by using the WAIS vocabulary subtest (Wechsler, 1955). In this task, the examiner asks the meaning of 40 words in ascending order of difficulty on the basis of frequency of use; results were expressed as *T*-scores. Vocabulary has been identified as the single best measure of premorbid IQ (Lezak, 1995).

One experienced psychiatrist (SAS) examined all subjects from a clinical perspective. All neuropsychological tests were administered by another physician (DJM) in a quiet testing room according to a standardized order.

Statistical analysis

The three groups (EO-BD, LO-BD, and healthy controls) were compared on clinical and demographic variables by using analysis of variance and Chi-squared as appropriate. Raw scores of neurocognitive tasks were transformed to standardized *Z*-scores from the normative data of each test in an attempt to diminish the confounding effect of age and years of education. In order to decrease the risk of type I errors because of the large number of analyses, one-way multivariate analysis of variance was conducted, with all neurocognitive measures as dependent variables and group membership (EO-BD, LO-BD, and healthy controls) as factor. It was suggested that because neuropsychological tests are naturally correlated, this procedure would be better than Bonferroni inequality correction that would increase the chance of type II errors (Torrent *et al.*, 2006). Differences between the three groups were analyzed with one-way analysis of variance, followed by Tukey post hoc comparison procedure when significant main effects were present. Pearson correlation coefficients were calculated to test for the associations between clinical–demographical variables, neurocognitive variables, and psychosocial functioning as measured by the GAF. The variables with significant correlation with psychosocial functioning (GAF) were considered as possible explanatory variables on a multiple linear regression model.

Results

Among EO-BD patients, age at illness onset was 29.22 (SD = 6.89) years, and length of illness was 40.06 (SD = 12.36) years. In the LO-BD group, age at illness onset was 53.78 (SD = 7.44), and length of illness was 15.50 (SD = 7.95) years. Clinical and demographical features of bipolar patients and healthy controls are shown in Table 1; no differences were found between groups in terms of age, gender, years of education, and subclinical symptoms (scores in YMRS and HDRS). Patients with LO-BD exhibited more severe extrapyramidal symptoms than healthy controls, whereas EO-BD patients did not differ significantly from either late-onset

Table 1 Clinical and demographical characteristics of bipolar patients and healthy controls (values are expressed as mean; standard deviation is shown in brackets)

	EO-BD (A)	LO-BD (B)	Controls (C)	Test	Group comparison (*p*-value)		
	(*n* = 20)	(*n* = 20)	(*n* = 20)	(*df* = 2)	A vs B	B vs C	A vs C
Age	69.10 (6.71)	66.90 (6.55)	70.50 (7.37)	$F = 1.38$, $p = 0.26$			
Gender (% female)	90	75	90	$X^2 = 2.35$, $p = 0.31$			
Years of education	11.30 (3.26)	10.35 (2.81)	10.85 (2.06)	$F = 0.59$, $p = 0.55$			
Premorbid IQ (*Z*-score)	0.19 (0.76)	−0.21 (0.50)	0.22 (0.25)	$F = 3.86$, $p = 0.026$	0.063	0.039	0.97
YMRS score	1.30 (1.69)	1.30 (1.92)	0.45 (0.51)	$F = 2.12$, $p = 0.13$			
HDRS score	1.80 (2.63)	2.10 (2.86)	2.23 (0.50)	$F = 0.32$, $p = 0.73$			
Prevalence of ES (*n*, %)	10 (50)	15 (75)	2 (10)	$X^2 = 17.34$, $p < 0.001$	0.102	<0.001	0.006
UPRS score	2.0 (2.53)	3.92 (3.93)	0.35 (0.93)	$F = 8.43$, $p = 0.001$	0.078	<0.001	0.15
GAF score	76.44 (12.78)	72.50 (9.87)	86.25 (4.02)	$F = 10.34$, $p = <0.001$ ($df = 1$)	0.449	<0.001	0.007
Previous hospitalizations	1.06 (1.81)	0.21 (0.58)		$F = 2.56$, $p = 0.12$			
Clinical subtype (% type II)	14 (70)	14 (70)		$X^2 = 0.00$, $p = 1.00$			
History of psychosis, *n* (%)	6 (30)	4 (20)		$X^2 = 0.53$, $p = 0.46$			

EO-BD, early-onset bipolar disorder patients; LO-BD, late-onset bipolar disorder patients; IQ, intelligence quotient; YMRS, Young Mania Rating Scale; HDRS, Hamilton Depression Rating Scale; ES, extrapyramidal symptoms; UPDRS, Unified Parkinson's Disease Rating Scale; GAF, General Assessment of Functioning.

BD patients or healthy controls (Table 1). No significant differences were found between patient groups in clinical subtype, history of psychosis, and previous hospitalizations. However, a significant difference between the groups in premorbid IQ (Table 1) was found, reason why it was included as a covariate in the one-way multivariate analysis of variance.

All patients were receiving psychotropic medications at the time of testing. There were no differences between patient groups in terms of exposure to mood stabilizers (EO-BD: 90% *vs* LO-BD: 85%; $X^2 = 0.23$, $df = 1$, $p = 0.63$), antipsychotics (EO-BD: 55% *vs* LO-BD: 50%; $X^2 = 0.10$, $df = 1$, $p = 0.75$), antidepressants (EO-BD: 50% *vs* LO-BD: 50%; $X^2 = 0.000$, $df = 1$, $p = 1.00$), and benzodiazepines (EO-BD: 55% *vs* LO-BD: 60%; $X^2 = 0.10$, $df = 1$, $p = 0.75$). Likewise, there were no differences between patients with early and late onset in doses of mood stabilizers [2.94 (0.57) *vs.* 2.78 (0.80), respectively; $df = 1$; $F = 0.36$; $p = 0.55$], antipsychotics [2.27 (0.90) *vs* 2.20 (0.78); $df = 1$; $F = 0.04$; $p = 0.85$], antidepressants [2.0 (0.66) *vs* 2.3 (1.06); $df = 1$; $F = 0.57$; $p = 0.46$], and benzodiazepines [2.45 (1.03) *vs* 2.17 (1.03), respectively; $df = 1$; $F = 0.45$; $p = 0.51$] as assessed by the IFD scale.

A significant overall difference in neurocognitive functioning between the groups was detected with multivariate analysis of variance (Pillai's $F = 2.02$; $df = 22, 88$; $p = 0.011$). For 8 of 11 comparisons, the differences reached statistical significance ($p < 0.05$); the group mean performance for each neurocognitive measure and the respective analysis of variance are presented in Table 2.

Table 2 Neurocognitive performance of bipolar patients and healthy controls (values are expressed as mean of *Z*-scores; standard deviation is shown in brackets)

	EO-BD (A)	LO-BD (B)	Controls (C)	Test	Group comparison (*p*-value)		
	(*n* = 20)	(*n* = 20)	(*n* = 20)	(*df* = 2)	A *vs* B	B *vs* C	A *vs* C
Immediate recall	−1.82 (2.09)	−2.95 (2.51)	−0.37 (1.23)	$F = 6.70$, $p = 0.003$	0.165	<0.001	0.056
Delay recall	−1.63 (1.96)	−3.03 (1.78)	−0.35 (1.03)	$F = 10.60$, $p = <0.001$	0.033	<0.001	0.045
Serial learning	0.87 (2.43)	0.25 (1.78)	2.25 (1.62)	$F = 3.47$, $p = 0.038$	0.457	0.004	0.086
Free delay recall	−0.74 (1.97)	−1.58 (1.78)	0.29 (1.54)	$F = 3.66$, $p = 0.032$	0.129	0.001	0.207
Recognition	1.52 (0.77)	1.21 (1.35)	1.78 (0.41)	$F = 1.40$, $p = 0.25$			
Boston Naming Test	−0.28 (1.31)	−1.41 (1.51)	−0.21 (0.67)	$F = 3.77$, $p = 0.029$	0.016	0.001	0.682
Forward Digit Span	−0.77 (1.10)	−1.01 (1.30)	−0.09 (1.10)	$F = 2.37$, $p = 0.10$			
Backward Digit Span	0.03 (1.13)	−0.16 (1.42)	1.06 (1.39)	$F = 3.42$, $p = 0.040$	0.891	0.013	0.043
Semantic fluency	−0.19 (1.42)	−1.06 (0.74)	−0.06 (0.74)	$F = 3.17$, $p = 0.050$			
Phonological fluency	−0.28 (0.75)	−0.59 (0.91)	0.41 (0.78)	$F = 5.85$, $p = 0.005$	0.109	<0.001	0.063
WCST perseverative errors	0.43 (1.22)	−0.32 (1.10)	1.30 (1.07)	$F = 6.88$, $p = 0.002$	0.077	<0.001	0.049

EO-BD, early-onset bipolar disorder patients; LO-BD, late-onset bipolar disorder patients; WCST, Wisconsin Card Sorting Test.

Within the EO-BD group, psychosocial functioning as assessed with the GAF was significantly associated with the presence of extrapyramidal symptoms ($R = -0.68$, $p = 0.002$) and measures of executive functions (Backward Digit Span: $R = 0.60$, $p = 0.008$; and perseverative errors on the WCST: $R = 0.64$, $p = 0.006$). When these variables were included in a linear regression model, both extrapyramidal symptoms ($\beta = -2.17$; $t = -2.41$; $p = 0.031$) and perseverative errors on the WCST ($\beta = 4.62$; $t = 2.57$; $p = 0.023$) were independent predictors of psychosocial functioning ($F = 10.77$, $df = 3$, $p = 0.001$). Likewise, within the LO-BD group, GAF score was significantly associated with extrapyramidal symptoms ($R = -0.50$, $p = 0.046$) and perseverative errors in WCST ($R = 0.64$, $p = 0.007$). Both UPDRS score ($\beta = -1.51$; $t = -2.31$; $p = 0.038$) and perseverative errors on the WCST ($\beta = 5.08$; $t = 3.24$; $p = 0.006$) were independent predictors of psychosocial functioning ($F = 9.27$, $df = 2$, $p = 0.003$) in a linear regression model.

Discussion

We have confirmed previous findings in older BD patients meeting strict euthymia criteria presenting with persistent impairments in verbal memory and executive functions (Gildengers *et al.*, 2007; Schouws *et al.*, 2007; Martino *et al.* 2008; Delaloye *et al.*, 2009a, 2009b). Our main finding was that patients with LO-BD had more extensive and severe neurocognitive impairments than those with EO-BD. Additionally, there was a trend to more extrapyramidal symptoms in the LO-BD group compared with the EO-BD and healthy control groups.

While EO-BD patients showed a poorer performance than healthy controls in two measures of verbal memory and two measures of executive functions, LO-BD patients delivered a lower performance than healthy controls on almost all measures assessed. Impairments within the LO-BD group included even neurocognitive domains such as naming (Boston Naming Test), typically preserved in mixed-age patients (Robinson *et al.*, 2006; Torres *et al.*, 2007), and differences in verbal memory (delay recall) compared with those within the EO-BD group. This finding agrees with a previous study that assessed EO-BD and LO-BD across a range of cognitive domains, which reported a more severely impaired performance in the LO-BD group (Schouws *et al.*, 2009). Likewise, patients with LO-BD display more extrapyramidal symptoms than healthy controls, and a trend to significance was found when compared with EO-BD patients. This result is particularly interesting, taking into account that it was reported that neurological signs may progress only minimally with increasing age in BD (Goswami *et al.*, 2007).

The results of this study are of theoretical and clinical importance. First, these findings provide additional data to the proposal of including age at onset as a subtype marker of BD (Bellivier *et al.*, 2003; Leboyer *et al.*, 2005). Additionally, the fact that LO-BD patients (with around 15 years of length of illness) have more extensive and severe cognitive impairments, as well as a trend to more extrapyramidal symptoms, compared with EO-BD patients (with around 40 years of length of illness) supports the hypothesis that different etiological mechanisms may be involved in the development of the illness in these subgroups. In contrast to genetic factors associated with EO-BD (Schürhoff *et al.*, 2000; Moorhead and Young, 2003; Depp and Jeste, 2004), different neuropsychiatric conditions have been targeted as possible brain mechanisms that might trigger the BD at an older age. In fact, a greater prevalence of vascular risk factors (Cassidy and Carrol, 2002) and higher prevalence of silent cerebral infarctions (Fujikawa *et al.*, 1995) have been reported in patients with LO-BD compared with patients with EO-BD. In addition, LO-BD patients have showed greater white matter hyperintensities of deep location (Ahn *et al.*, 2004), and white matter hyperintensities might be associated with neurocognitive impairments — executive functioning, attention, verbal memory, and information processing speed — and physical disability due to reduced speed, fine motor coordination, and muscular strength (Gunning-Dixon and Raz, 2000; Burton *et al.*, 2004; Sachdev *et al.*, 2005). On the other hand, case series were also recently reported, suggesting that different neurodegenerative diseases, such as frontotemporal dementia and Alzheimer's disease, at early stages would simulate symptoms of bipolar disorder (Ng *et al.*,. 2008; Velakoulis *et al.*, 2009). The possibility that LO-BD is in fact the first stage of frontotemporal dementia is reinforced by the possible overlapping of clinical data, neuropsychology, and neuroimaging (Rascovsky *et al.*, 2011). In other words, in some patients (i.e., patients with history of subthreshold manifestations of BD), the beginning of the neurodegenerative process would manifest as an LO-BD in a prodromal stage, whereas core features would emerge later with the progress of physiopathological mechanisms of the illness.

Taken together, LO-BD would be a heterogeneous population composed of patients with a primary BD beginning in a late age and other patients in which psychiatric symptoms emerge as a consequence of a

neuropsychiatric illness. In other words, at least some LO-BD may display clinical manifestations of BD when different underlying neuropsychiatric conditions began to develop interfering with frontolimbic circuits involving the prefrontal cortex, medial temporal lobe, and striatum (regions anatomically related with the pathophysiology of EO-BD) (Zanetti *et al*., 2007). This would be particularly true for patients with history of subthreshold manifestations of BD, as those with antecedent of isolated hypomanic episodes or hyperthymic/cyclotymic temperaments (Dorey *et al*., 2008). However, if it was the case, the outcome of illness would be dominated by the progress of neuropsychiatric illness with further cognitive impairments and behavioral-functional decline more than by affective symptoms in this subgroup of patients. However, up to date, this perspective is speculative, and further longitudinal studies comparing neuroimaging brain changes and neurocognitive decline of EO-BD and LO-BD would be useful to explore this hypothesis. Clinically, the possibility of other neuropsychiatric conditions, such as cerebrovascular or neurodegenerative diseases, underlying LO-BD suggests the need for a throughout clinical evaluation and construction of a comprehensive diagnosis in all such cases. Use of a neuropsychiatric approach, including elements of psychiatric and neurological interviews, as well as neurocognitive, laboratory, and neuroimaging studies, is thus strongly recommended for these patients.

Another finding of our study was that in both EO-BD and LO-BD, psychosocial functioning was associated with executive functioning as well as with extrapyramidal symptoms more than with subclinical symptoms or chronicity illness measures. These results agree with previous studies in young (Goswami *et al*., 2006) and older (Martino *et al*., 2008) patients with euthymic BD. Our findings suggest that cognitive–motor disturbances may help to explain the impairments in daily functioning among older patients with EO-BD and LO-BD during remission and could have clinical implications if they are in fact confirmed by further studies. First, the routine assessment of these features could be necessary in clinical practice. Second, these patients may benefit from neuropsychological rehabilitation and from caution in the use of drugs that can increase extrapyramidal symptoms in order to minimize the effect of cognitive and motor disturbances on their overall functioning.

Some limitations in our work need to be acknowledged. A larger sample size could have demonstrated clearer differences between EO-BD and LO-BD in extrapyramidal symptoms and neurocognitive performance. Furthermore, all patients were taking psychotropic medications, and the effects of these medications cannot be excluded altogether from the interpretation of the findings. However, it may be difficult to interpret that differences between EO-BD and LO-BD in our study rely on medications patterns because both patient groups were paired in terms of exposure to different type and doses of psychotropic medications. Finally, the cross-sectional design does not allow for the examination of the stable or progressive nature of cognitive impairments and extrapyramidal symptoms in these populations.

In summary, our study brings preliminary evidence that patients with LO-BD would have more extensive and severe cognitive impairments and extrapyramidal symptoms compared with those with EO-BD. Age of onset of illness may be useful in explaining the heterogeneity of older patients with BD. Cognitive impairments and extrapyramidal symptoms could be a component of disability in daily functioning among these patients.

Conflict of interest

None.

Key points

- Patients with late-onset bipolar disorder have more extensive and severe neurocognitive impairments than patients with early-onset bipolar disorder.
- Likewise, late-onset patients showed a trend to higher extrapyramidal symptoms than those with early onset.
- These results suggest that age at onset would contribute to explain heterogeneity between older patients with bipolar disorder.

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