Original article

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Cognitive functioning in patients with schizophrenia and bipolar disorder under chronic treatment: an observational study

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Summary

Objective

Clinical practice usually considers schizophrenia and bipolar disorder as two distinct nosological entities. Nevertheless, research over the past decades has shown similar impaired cognitive profiles in patients with schizophrenia and bipolar disorder. The objective of the present study was to verify whether the diagnostic distinction between these disorders effectively accounts for clinical, cognitive and functional profiles.

Materials and Methods

42 patients (mean age 44.3; 36% female), with diagnosis of schizophrenia (n = 23) or bipolar disorder (n = 19) in charge of an outpatient psychiatric public service were recruited. Cognitive abilities were measured with the MCCB. Clinical (BPRS, CGI) and functional (VGF, QL-index) scales were also administered. Linear regressions were conducted investigating whether the diagnosis could predict neurocognitive outcomes and examining the effects of neurocognitive performances on functional outcome.

Results

Both groups showed comparable performances in all cognitive domains and diagnosis was not a significant predictor of any cognitive variable. Moreover, lower scores in working memory and speed of processing predicted worse functioning.

Conclusions

The present findings support the perspective of a continuum between schizophrenia and bipolar disorder and further underline the importance of neurocognitive examination in psychiatric diseases, in light of its fundamental role in predicting daily functioning.

Key words

Cognition • Psychosis • Schizophrenia • Bipolar disorder • MATRICS

Introduction

Current psychiatric classification still refers to the so called "Kraepelinian dichotomy" between schizophrenia (SZ) and bipolar disorder (BD), which consider these two illnesses as separate nosological entities. Nevertheless clinical practice often clashes with this strict categorical approach. Findings from various areas of research, including neuroimaging, neuropathology and molecular genetics, have demonstrated the inadequacies of the dichotomous view, and highlighted the importance of better classifying cases with both psychotic and affective symptoms [1]. There is a growing consensus regarding the importance of incorporating cognitive deficits into the major diagnostic systems [2,3]. Research in SZ over the past decades has shown a global cognitive impairment, which involves memory, attention, executive functions, language and intelligence [4,5]. In the last years cognitive deficits have also been found in BD [6-8]. Data indicate that these deficits are prominent during acute depressive and manic episodes

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but do not entirely resolve between episodes [9], and that these persistent deficits may contribute to the development of functional impairment in BD patients.
A recent review comparing cognitive impairment in SZ and BD reported that overall patients share similar impaired cognitive profiles, albeit with different degrees of deficits [10]. In particular, individuals with SZ show more severe and pervasive cognitive deficits in comparison with individuals with BD, which present a milder and more confined impairment. The difference between these groups of patients seems therefore to be quantitative rather than qualitative.
Significant overlap is observed in both SZ and BP also in social cognitive performance deficits, affecting the capacity to recognize facial expressions of emotions and to infer the mental states of others [11 12]. For instance, in a recent study both SZ and BD groups showed extensive impairment in social as well non-social cognitive domains when assessed in an ecological context, although SZ performances resulted worse than BD in the majority of the investigated domains [13].
Another study compared cognitive performances of individuals with SZ and BD and their relatives: the authors found a generalized cognitive impairment in multiple domains, again more pronounced in SZ and less consistent in BD [14].
On the other hand there is a large literature reporting no differences in neurocognition between these diagnostic groups [15-18] or differences in some measures but not in others [19 20].
Whether SZ and BD can be distinguished on the basis of their cognitive performances still remains a matter of debate. The high variability across studies, and in particular the heterogeneity in the choice of neuropsychological instruments adopted to test cognitive abilities, hampers generalization of results. The Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) Initiative developed a consensus cognitive battery (MATRICS Consensus Cognitive Battery - MCCB) assembled to assess key cognitive domains in SZ [21 22]. Recent findings suggest that the MCCB, together with additional measures of executive functions, may represent a promising consensus-based tool also in cognitive trials for BD [23-26].
Cognition in psychotic disorders needs further research, not only for its role in the debate about categorical and dimensional psychiatry, but also for its importance in clinical practice. In fact, there is evidence of a relationship between cognition, symptoms and functional capacity in psychotic disorders [27 28], suggesting that cognitive performance appears as a fundamental longitudinal predictor of functioning [29]. The objective of the present study was to contribute to expand the exisiting literature about similarities and differences between SZ and BD and to study whether the actual diagnostic distinction effectively accounts for clinical, cognitive and functional profiles of patients in the context of clinical practice. In particular, cognitive characteristics of outpatients with SZ or BD under chronic treatment were assessed by means of the MCCB, and the relationships between neurocognitive performances, clinical features and everyday functioning were investigated.

Methods

Participants

Forty-two patients with diagnosis of SZ (n = 23; 55%) and BD (n = 19; 45%) were recruited in an outpatient psychiatric public service of ASST Fatebenefratelli-Sacco Hospital in an urban area of Milan (Italy). Participants were between the ages of 19 and 71 (mean age 44,3, s.d. 12,1); 64% were male, 36% female.
All participants were patients in treatment at a daily outpatient service. Inclusion criteria were a current diagnosis of SZ or BD (including BD I, BD II and BD NOS) according to the ICD-10 classification system, age ≥ 18. Exclusion criteria were recent acute psychotic, depression or mania episodes, mental retardation or other neurological brain diseases, current substance, alcohol or benzodiazepines abuse or dependence. Informed consent was obtained for the participation in the study, performed in accordance with the Declaration of Helsinki. All patients gave their written informed consent to the processing of personal information.

Materials

All participants were administered the following clinical scales: the Brief Psychiatric Rating Scale (24 items) [30]; the Clinical Global Impressions (CGI) [31]; the Quality of Life Index (QL-Index) [32]; the Global Assessment of Functioning (VGF) [33]
Neurocognitive and social cognitive assessment were conducted through the administration of MCCB (Italian Language version, provided by MATRICS Assessment INC), including the following domains: speed of processing (Trail Making Test A, Brief Assessment of Cognition in Schizophrenia, Symbol Coding, Category Fluency), attention/vigilance (Continous Performance Test: Identical Pairs), working memory (Wechsler Memory Scale Spatial Span, Letter Number Span), verbal learning (Hopkins Verbal Learning Test), visual learning (Brief Visuospatial Memory Test), reasoning/problem solving (Neuropsychological Assessment Battery: Mazes), social cognition (Mayer-Salovey-Caruso Emotional Intelligence Test: Managing Emotions).
Clinical and cognitive assessments were conducted in the same day. Trained psychiatrists managed clinical assessment and therapy, and the administration of clini-

cal scales. Thereafter, a trained psychologist administered the MCCB.

Statistical analysis

Results of neurocognitive tests of MCCB, both for the composite score and for sub-test scores, were reported as t-scores. Data were analyzed using SPSS package (SPSS Statistics 23, IBM Corporation 1989, 2015). Comparisons of demographic, clinical and neurocognitive variables were performed with independent sample t-tests and chi-square analysis. Linear regressions were conducted to examine the effects of diagnosis on neurocognitive outcomes. Demographic variables were also included in the linear regression model. Linear regressions were then performed to examine the effects of neurocognitive performances on functional outcome (QL-Index, VGF) while covarying for clinical variables (BPRS and CGI).

Results

SZ and BD groups differed on age (p = 0.003), age of onset (p = 0.003) and duration of AP treatment (p < 0.001). The other examined demographic characteristics (gender, education and duration of illness) were not significantly different between groups (Table I). Clinical assessment showed significant differences between groups. SZ obtained higher scores in comparison to BD in BPRS (p = 0.009) and CGI (p = 0.036), and lower scores in VGF (p = 0.028). No significant difference was observed in QL-index (Table I).

As regards to neurocognitive examination, a look at percentile scores of both groups revealed that all patients showed poor performances in all domains of MCCB. In particular, SZ group performed below 1.5 *sd* in the subtest Speed and Attention, while both groups performed below 1.5 *sd* in Social Cognition in the composite score (Table II).

Interestingly, although percentile scores obtained by SZ group were overall lower than percentile scores obtained by BD group, statistical comparisons performed on t-scores revealed that SZ and BD obtained comparable results in the composite score and in all sub-test scores of MCCB, with a lack of significant differences between groups (Table II, Fig. 1).

The effects of diagnosis on neurocognitive outcomes were analyzed with linear regressions, which revealed that the diagnosis was not a significant predictor of any cognitive variable. When including all demographic variables in the regression model, results showed that the lower level of education predicted worse cognitive functioning in the following subscales: Speed (t(41) = 2,71, p = 0,010), Attention (t(41) = 2,24, p = 0,031), Working Memory (t(41) = 3,08, p = 0,004), Verbal Memory (t(41) = 2,15, p = 0,039), Composite (t(41) = 2,98, p = 0,005). Gender was a predictor of Reasoning score (t(41) = -2,42, p = 0,021), with males performing better and longer duration of AP treatment predicted lower verbal memory performances (t(41) = -2,34, p = 0,025). Finally, linear regressions were performed to analyze whether cognitive functioning can predict community functioning while covarying for clinical symptomatology. Results indicated that lower scores obtained in Working Memory subtest was a significant predictor of lower VGF scores (t(41) = 2,423, p = 0,020) and lower Speed of performance predicted lower QL-index (t(41) = 2,064, p = 0,046).

TABLE I. *Demographic and clinical characteristics of schizophrenic and bipolar groups*

	SZ (n = 23)	BD (n = 19)	Statistics
Age (y)	39,4 ± 10,5	50,3 ± 11,4	t = -3,21 p = 0,003
Gender (female)	8 (42,1)	7 (30,4)	χ^2 = 0,62 n.s.
Education (y)	13,8 ± 3,1	13,1 ± 4,2	t = 0,60 n.s.
Age of onset (y)	25,9 ± 7,9	37,5 ± 15,2	t = -3,18 p = 0,003
Duration of illness (y)	12,7 ± 11,2	13,5 ± 9,5	t = 0,23 n.s.
AP treatment (y)	11 ± 7,4	2,8 ± 6,5	t = -3,84 p < 0,001
BPRS (%)	60,1 ± 16,2	46,7 ± 14,1	t = 2,82 p = 0,007
CGI (%)	4,3 ± 1,1	3,6 ± 1	t = 2,16 p = 0,036
VGF (%)	59,9 ± 18,7	71,6 ± 13,7	t = -2,28 p = 0,028
QL-index (%)	5,8 ± 2,6	6,5 ± 2,3	t = -0,90 n.s.

Values are presented as mean ± standard deviation (sd) or number. y = years; AP = antipsychotic.

Discussion

The present study examined the clinical, functional and neurocognitive characteristics of outpatients with SZ or BD. Results revealed that the two groups show different clinical features, but they share common neurocognitive impairments. Only education modulated cognitive performance on several subtest and the duration of AP treatment, which may be related to the severity of illness, had an impact on verbal memory performances. In addition, regression analyses revealed that cognitive deficits in the domain of working memory and speed of

TABLE II. *Neurocognitive evaluation of schizophrenic and bipolar groups.*

MCCB	Percentiles		t-scores		Statistics
	SZ (n = 23)	BD (n = 19)	SZ (n = 23)	BD (n = 19)	
Speed of processing	*9,4 ± 11,9	17,3 ± 24,1	31,4 ± 10,3	35,1 ± 12,3	t = -1,08 n.s.
Attention/Vigilance	*12,2 ± 17,6	21,1 ± 22,6	32,3 ± 12,3	35,8 ± 14,1	t = -0,85 n.s.
Working memory	25,6 ± 25,5	25,5 ± 22	40,7 ± 10,2	41,1 ± 9,4	t = -0,13 n.s.
Verbal Learning	28,7 ± 26,1	31,5 ± 24,3	42,6 ± 9,4	43,3 ± 9	t = -0,24 n.s.
Visual learning	37,2 ± 35,4	34,1 ± 33,7	41,4 ± 16,6	42,4 ± 15,2	t = -0,19 n.s.
Problem Solving	36,9 ± 33,8	42 ± 28,3	44,9 ± 11,8	47,6 ± 9,3	t = -0,80 n.s.
Social Cognition	*8,5 ± 14,2	*12,4 ± 15,6	30 ± 10,8	32,1 ± 13,3	t = -0,58 n.s.
Composite	*9,8 ± 12,9	*15,3 ± 19,4	29,9 ± 12,9	32,9 ± 14,3	t = -0,73 n.s.

Values are presented as mean percentiles and t scores ± standard deviation. Statistics are referred to t-scores.
** Asterisks indicate scores below the 16th percentile*

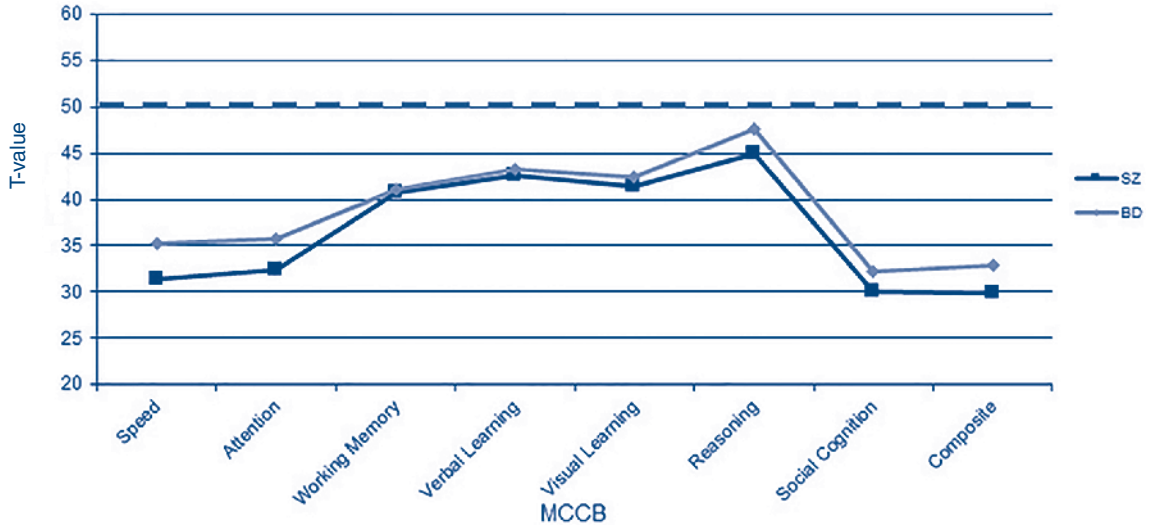

FIGURE 1. *Performances of SZ and BD groups (T-scores) in MCCB subtest and composite score. Both SZ and BD showed poor performances, with scores below the mean t-score (dotted line) in all sub-tests of the MCCB and in the composite score, without any significant statistical difference between groups.*

processing are closely related to everyday functioning.
In the last decade a sustained debate has grown about the need to rethink psychiatric classification systems, to account for increasing evidence of discrepancies between the categorical approach of the diagnostic classifications and the observations of everyday clinical practice (see for example the Research Domain Criteria Project) [34]. Kraepelinian division of major psychoses into dementia praecox (later identified as SZ) and manic depressive psychosis (BD) is now subject matter of discussion. Recent literature comparing SZ and BD actually redefine these psychiatric disorders as lying along a continuum of psychotic disorders [20] as confirmed by the results of numerous neurobiological investigations, which indicate common genetic susceptibilities [35] and neuroanatomical and neurochemical similarities [36]. In fact, findings from the large-scale Bipolar-Schizophrenia Network on Intermediate Phenotypes (B-SNIP) Study, comparing social and cognitive deficits across psychotic proband groups and their first-degree relatives, indicate the existence of a continuum of severity underlying psychotic disorders, ranging from BD to SZ [37].
Neurocognitive impairments have been reported to be one of the core symptoms in SZ and growing literature is demonstrating that cognitive deficits are consistent

also in BD along the course of illness [38]. Nevertheless, it is still matter of debate whether individuals with SZ and BD show impairments in the same cognitive domains and with the same severity, so that an increasing number of studies is searching for boundaries able to discriminate between these psychopathologies.

Results from the present study, indicating common neurocognitive deficits in SZ and BD, substantially support the perspective of a continuum between these disorders. Specific features of the sample composition could have influenced our results. In particular, it has to be noted that all participants were recruited in the context of an outpatient psychiatric public service [39], where more disabling conditions assemble. It can be supposed that our sample was constituted by highly severe pathologies and that this condition interfered with the emergence of eventual subtle differences in cognitive abilities between SZ and BD groups. Nevertheless, our groups of patients significantly differed in terms of severity of illness as revealed by clinical assessment and by the length of AP treatment. The overlap between cognitive performances of BD and SZ found in this study could be ascribed to a particular subgroup of patients with BD in our sample presenting more pronounced cognitive deficits. In fact, Burdick and colleagues [6] found evidence for three distinct, cognitively homogeneous subgroups in a wide sample of BD patients, ranging from normal cognitive functioning like healthy controls, to severe cognitive impairment comparable to SZ patients.

Other characteristics of the sample could have interfered with our results. In fact, our groups of patients significantly differed on several demographic characteristics (age, age of onset), which can significantly influence cognitive performances. Indeed, neuropsychological deficits have been documented to be more pronounced among older relative to younger individuals with BD [40]. In addition, it has been documented that later onset of SZ is related to better social cognition, whereas patients' older age is related to a worse performance across multiple cognitive domains [41].

The present study further underline the importance of neurocognitive examination in psychiatric diseases, in light of its fundamental role in predicting daily functioning. In fact our results evidence that not only the severity of clinical symptomatology can affect community functioning, but also cognitive deficits in the domain of working memory and speed of processing are highly predictive of worse levels of global functioning and lower indexes of quality of life.

This finding is in line with previous studies which evidenced that neuropsychological performance seems to be a fundamental longitudinal predictor of functioning in both disorders [28 42], even separately from mood symptomatology [43-46]. These results also suggest that the inclusion of the cognitive dimension in the assessment of severe mental disorders could facilitate the introduction of therapeutic and rehabilitative strategies more effective and strictly related to everyday difficulties encountered by patients.

It is noteworthy that in the present research cognitive functioning was assessed by the administration of the MCCB. The majority of previous studies comparing SZ and BD populations employed different cognitive batteries and the heterogeneity of measures employed in the past may account for differences in findings [20]. The adoption of cognitive assessment batteries specifically developed for individuals affected by severe mental disorders could help future research to better discriminate differences and commonalities among psychiatric populations.

The results of the current study are to be considered in light of some limits. The influence of negative symptoms was not controlled for and the limited sample size might have biased results, in particular because all patients were recruited out of acute episodes, but in treatment at a daily outpatients service. This underlines the severity of bipolar disorders included and would require higher numbers to validate, without bias risk, the hypothesis of an overlapping in cognitive performances of the two samples. Moreover, the need for antipsychotic therapy in bipolar disorders may be related to the severity of illness, due to the fact that this is more frequently prescribed in patients with mood episodes with psychotic features, in particular manic episodes. This might be a negative marker, in particular among patients with multiple episodes, of a possible subtype of bipolar disorder more related to cognitive deterioration or in relationship to the total amount and/or lenght of antipsychotic treatment. In this study we analyzed the effect of antipsychotic treatment length, but data on number and polarity or quality (psychotic/non psychotic) episodes or cumulative antipsychotic doses were not available. Nevertheless, the current study expands upon previous investigation thanks to its adherence to "real-world" mental illness, with data coming from patients with long history of disease in charge of an outpatient psychiatric public service, to be considered as a value in terms of clinical relevance [47].

In conclusion, we found that SZ and BD showed similar cognitive impairment and that cognitive profile can predict actual functioning and quality of life independently from clinical symptomathology. We can argue that patients with BD received in the context of psychiatric public services probably represent a subgroup characterized by a severe cognitive impairment not different from patients with SZ. These findings are in accordance with the current hypothesis about the existence of a spectrum of neurocognitive impairments across psy-

chotic diseases and support the development of a "dimensional psychiatry" using cognitive phenotypes as markers of independent subgroups across diagnostic boundaries [42]. Our findings also suggest that cognitive disabilities should be considered as essential factors in clinical practice for their relevance in everyday functioning and in a better definition of the needs of care and efficacy of treatments undertaken in psychiatric services.

Conflict of interest

None.

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