Psychiatry Research 272 (2019) 551–554

Contents lists available at ScienceDirect

Psychiatry Research

journal homepage: www.elsevier.com/locate/psychres

Short communication

Social cognition in first episode bipolar disorder patients

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ARTICLE INFO

Keywords:
Social cognition
First-episode
Bipolar disorder

ABSTRACT

The aim of this study was to describe theory of mind (ToM) and emotional processing (EP) functioning in recently diagnosed bipolar disorder (BD). We evaluated 26 first episode BD (mean age 22.9 ± 7.4) and 26 controls matched on age, gender, education, and premorbid intelligence. A significant poorer performance on the capacity of patients to infer other's intentions (cognitive ToM) that was partially independent from neurocognitive deficits ($p < 0.01$) as well as a lower recognition of fear was observed among patients. No significant association between any of these deficits and psychosocial functioning emerged in multivariate regression analyses.

1. Introduction

The presence of neurocognitive dysfunction in bipolar disorder (BD) has been well established in the literature. Deficits in attention, verbal memory, and executive functions are found in BD patients, even during periods of euthymia (Mann-Wrobel et al., 2011), and these alterations are known to be present since the first episode of the illness (Bora and Pantelis, 2015; Lee et al., 2014). Conversely, research on social cognition in BD is scarce, and investigations have traditionally focused on two central processes: theory of mind (ToM) and emotional processing (EP). The first meta-analysis of social cognition in euthymic BD patients have found that - in comparison to healthy controls -, patients had impairments of moderate magnitude in ToM and of small effect size in EP (Samamé et al., 2012). Nevertheless, to the date, there has been no studies addressing this issue in first-episode BD patients. This would be of special interest in order to determine the onset of such deficits: whether they are present since the beginning of the condition (i.e., as primary deficits) or whether they emerge as the disease goes on, as a consequence of the development of other factors such as pharmacological exposure, neurocognitive deficits, or the stigma associated with multiple episodes (i.e., as secondary deficits).

Finally, literature addressing psychosocial implications of social cognitive deficits in BD has yielded so far mostly negative results (Barrera et al., 2013; Martino et al., 2011). However, this relationship has been studied in samples of multiple-episode patients and a relationship between these domains in patients at the moment of their diagnosis has not been explored yet.

The main objective of the present study was to investigate the performance on social cognitive tasks of a sample of patients with a first manic episode. Also, we explored whether social cognitive functioning was associated with psychosocial outcomes.

2. Methods

Twenty-six patients meeting MINI-International Neuropsychiatric Interview criteria for Bipolar Disorder type I – presenting their first manic episode (FEM) - were recruited as a part of a program to assess longitudinal evolution of this condition at the Torcuato de Alvear Psychiatric Emergencies Hospital, in Buenos Aires, Argentina: FEPA program. Further details about recruitment can be found elsewhere (Szmulewicz et al., 2018). Patients enrolled in this program are allowed to have previous depressive episodes as long as their diagnosis was other than BD and the current manic episode was the one that established their BD diagnosis. Patients were assessed weekly and after achieving defined criteria for syndromatic remission (Young Mania Rating Scale -YMRS- ≤6 and Hamilton Depressive Rating Scale -HDRS-

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https://doi.org/10.1016/j.psychres.2019.01.002
Received 8 October 2018; Received in revised form 10 December 2018; Accepted 1 January 2019
Available online 03 January 2019
0165-1781/

≤8) underwent neurocognitive and social cognitive assessment. Exclusion criteria included a history of head injury or neurological disease. A convenience sample of twenty-six healthy participants was contacted from the community, using age-group, gender and education as selection criteria. Controls were also assessed to discard family history of psychiatric disorders and a personal history of psychotropic medication use.

Ethics approval was received and all patients included provided written informed consent.

2.1. Clinical and functional assessment

Patient's mood was formally assessed using YMRS and HDRS. Course of illness prior to the current manic episode was evaluated through direct patient interviewing and revision of the medical chart. When possible, attempts were made to verify this data with a family record.

Baseline functional and social status was evaluated using the Functional Assessment Short Test (FAST) (Rosa et al., 2007) after having reached the syndromatic remission. Patients were asked to respond to this scale on the basis of their functioning previous to the manic episode and/or hospitalization.

Pharmacological load was assessed by means of the Clinical Scale of Intensity, Frequency, and Duration of Psychopharmacological Treatment (IFD) that provides a quantitative measure of exposure to psychotropic agents in a 0–5-point range.

2.2. Neurocognitive assessment

Neurocognitive tests were selected on the basis of neurocognitive domains usually associated with a proper accomplishment of the social cognitive battery (Bora et al., 2016; Martino et al., 2011). Accordingly, tests evaluating the domains of attention (WAIS-III forward digit span), working memory (WAIS-III backward digit span), cognitive flexibility (trail making test B), and processing speed (trail making test A) were selected. Finally, premorbid intelligence was assessed by means of the WAIS-III vocabulary subtest.

2.3. Social cognition assessment

We evaluated the social cognitive domains of theory of mind and emotional processing as these were the more consistently documented in BD patients (Bora and Pantelis, 2016; Samamé et al., 2015, 2012). The mind in the eyes test (MIE) was used to evaluate ToM (Bechara et al., 1997). It is a computerized task in which patients are shown 36 photographs of the eye region of faces and are asked to choose between 4 options the best word that describes what the individual in the picture is thinking or feeling and also were asked to inform the sex of the photographed face. This task is sensitive to subtle ToM deficits since it involves recognition of complex mental states. Total ToM score was obtained.

Faux-Pas test (FPT) evaluates also ToM (Baron-Cohen et al., 1997). In this task, the individual is read 20 stories that may or may not contain a social faux pas. After each story, the subject is asked whether something inappropriate was said and if so, why. To realize that a faux pas occurred, the subject has to represent two mental states. First, that the ones committing the faux pas are unaware they have said something inappropriate, and second, that the person hearing it might feel hurt or insulted. Hence, this task evaluates a cognitive (Why do you think they said it?) and an affective component (why they shouldn't have said it?) of ToM. The test includes also an additional memory question. For the purpose of the present study, we calculated an affective index with the numbers of faux pas correctly identified or rejected, and the recognition of the person involved in the social faux pas, and a cognitive index, with the correct answer to the questions “why” (Heitz et al., 2016; Roca et al., 2014; Torralva et al., 2015). The total ToM score includes both indexes.

The Ekman test was used to evaluate EP. It is a computerized test that includes 60 photographs of different individuals displaying facial expressions of six basic emotions (sadness, happiness, anger, fear, disgust, and surprise). The photographs stay on the screen for 5 s and the participants has to choose one of these six basic emotions. Total scores and sub scores for each individual emotion were obtained.

2.4. Statistical analysis

Quantitative variables are presented as mean and standard deviation, or, in case of noticeably skewed data, as median and interquartile range. Baseline differences in demographical and neurocognitive measures between patients and controls were assessed using chi-square test for categorical variables and student's *T* test for continuous variables. The comparison of the Faux-Pas total score, affective, and cognitive indexes, the reading-in-the-eyes total score and the Ekman total score as well as each individual emotion sub-score were performed with Student's *T* Test. When normal distribution of the variables could not be achieved even after log transformation of the data, non-parametric Wilcoxon test was performed.

Finally, we explored the dependence of social cognitive variables on neurocognitive results using correlation tests. In order to evaluate the effect of social cognitive on functional outcomes, we fitted multiple regression models adjusting for neurocognitive variables proven significant in correlation analyses as well as premorbid IQ and education levels. All analyses were performed using STATA v.14.0.

3. Results

3.1. Demographical, clinical, and neurocognitive characteristics of the sample

All patients included presented a manic episode with psychotic features and were medication-free at the time of disease onset. Thirteen patients of the total sample (50.0%) were hospitalized due to the severity of their manic episode. Five patients presented a previous depressive episode (19.2% of the sample) but only one patient was hospitalized in his/her previous depressive episode and was diagnosed as MDD. Median time from manic episode to neuropsychological assessment was 2 months with an interquartile range from 2 to 4 months. At the time of the neuropsychological assessment, patients had a mean YMRS of 2.0 (SD:2.2) and a HDRS of 1.3 (SD:1.9) points, and 61.5% were receiving lithium, 84.6% antipsychotics, and 23.1% benzodiazepines. Mean score and SD for the IFD scale for benzodiazepines, mood stabilizers and antipsychotics were: 0.65 (1.33); 2.23 (1.34) and 2.19 (1.17) respectively.

Patients and controls were successfully matched on age, gender, education, and premorbid intelligence (Table 1). FEM patients underperformed controls on measures of attention, processing speed, and executive functioning (Table 1).

3.2. Social cognitive performance and association with neurocognitive variables

Reading EP processes, we found no significant differences between patients and controls in net total Ekman scores (t statistic = 1.79, $p = 0.08$) (Table 1) or in individual emotion recognition, except for a significant lower fear recognition in patients (t statistic = 2.89, $p = 0.01$). We found no significant association between EP processing and any neurocognitive variables (all R's P values > 0.10).

We could not detect any significant difference on the MIE test between patients and controls (Table 1). However, we did find that patients underperformed significantly controls on the Faux-Pas test (t-statistic = 4.15, $p < 0.001$). When we analyzed separately affective and cognitive sub scores of the Faux-Pas test, we found no significant

Table 1
Demographic features, and neurocognitive and social cognitive performance of patients and healthy controls.

Characteristic	Patients (N = 26)	Healthy controls (N = 26)	p value[a]
Age - years (mean, SD)	22.9 (7.4)	25.7 (5.2)	0.13
Male sex – (%)	69.2	50.0	0.26
Premorbid IQ (mean Z-score; SD)	0.1 (0.7)	0.3 (0.7)	0.38
Education, years (mean; SD)	12.7 (2.6)	13.7 (2.7)	0.21
Functional features			
FAST total score (mean; SD)	17.6 (8.0)	7.6 (5.2)	<0.001
Neurocognitive Functioning			
Trail-Making test A (Z score; SD)	0.8 (0.8)	1.4 (0.7)	0.01
Direct digit span test (Z score; SD)	−0.6 (1.3)	0.4 (1.3)	0.01
Indirect digit span test (Z score; SD)	0.3(1.2)	0.7 (1.3)	0.37
Trail Making test B (Z score; SD)	−0.3 (1.4)	0.8 (0.9)	0.002
Emotion processing			
Ekman total score (raw score, SD)	45.2 (5.4)	48.0 (5.3)	0.07
Anger score (raw score, SD)	7.2 (1.8)	7.2 (1.5)	0.85
Surprise score (raw score, SD)	9.0 (1.1)	9.4 (0.9)	0.16
Sadness score (raw score, SD)	6.7 (2.2)	7.4 (2.2)	0.26
Happiness score (raw score, SD)	9.8 (0.4)	9.7 (0.5)	0.51
Disgust score (raw score, SD)	7.9 (1.6)	7.7 (1.7)	0.66
Fear score (raw score, SD)	4.6 (2.8)	6.6 (2.2)	0.02
Theory of mind – Mentalizing skills			
Total ToM (raw score, SD)	30.8 (4.7)	35.8 (3.5)	<0.001
Affective sub-score (raw score, SD)	26.1 (2.3)	26.7 (3.6)	0.56
Cognitive sub-score (raw score, SD)	5.2 (2.2)	8.0 (1.7)	<0.001
RMET (raw score, SD)	20.5 (4.7)	22.4 (2.8)	0.10

RMET: reading the mind in the eyes test, SD: standard deviation, FAST: Functioning Assessment Short Test, ToM: theory of mind; IQ: intelligence quotient.

[a] Two-sided p values. Means are compared with Student's T-test, and proportions with the Fisher's exact test.

differences in the affective recognition performance while a strong significant lower cognitive performance in the Faux-Pas (t-statistic = 4.76, $p < 0.001$). Finally, a significant correlation between direct digit span and the cognitive sub-score of the Faux-Pas test was detected ($r = 0.41$, $p = 0.01$). In fact, differences between patients and controls were attenuated after controlling for this neurocognitive variable but persisted significant (β coefficient: −4.07, 95%CI: −5.52 to −2.62, $p < 0.001$). None of the neurocognitive measures correlated significantly with the affective component of ToM (all R's P value > 0.10).

3.3. Relationship with functional outcomes

No associations between functional outcomes and performance on ToM tests (total Faux-Pas score) emerged on the multivariate model adjusted by premorbid CI, education, and direct digit span performance (β coefficient 0.21; 95%CI −0.6 to 1.02; $p = 0.60$). Finally, none of the EP results showed significant associations with functional scores.

4. Discussion

The main findings of this study were that BD patients recovered from their first manic episode showed an impaired performance on the Faux-Pas task and lower recognition of fear. These results agree with those of the largest systematic review on this topic that reported deficits in ToM tasks and emotional processing in BD (Samamé et al., 2012), making them extensive to the early stages of the illness. Contrary to such meta-analysis, we found no differences between patients and controls in complex mindreading tasks. However, it is important to note that also individual studies in samples multiple-episode BD patients showed controversial results in MIE performance, with some showing alterations (Bora et al., 2005) and others a performance similar to that of healthy controls (Martino et al., 2011).

Regarding the Faux-Pas task, patients were significantly less able to infer intentions from others (showing a compromised cognitive ToM performance) while their capacity to detect other's emotions and feelings were overall intact (showing a normal affective ToM performance). This finding could suggest that an altered capacity to infer other's intentions is inherent to BD and present since the disease's onset. This could also explain why patients could correctly detect complex mental states such as those shown in the Mind in the Eyes Reading Task, underlining the finding of an intact affective ToM performance. This dissociation between affective and cognitive ToM processes was described in others neuropsychiatric conditions (Roca et al., 2014; Torralva et al., 2015) and there is growing evidence suggesting that both components could depend on different brain networks, being the cognitive component reliant on frontal-medial cortex, while the affective component relies on orbitofrontal and temporal cortex (Lee et al., 2004; Sabbagh, 2004).

Another main finding of our study was that there was no relationship between social cognitive and psychosocial outcomes in first-episode BD patients. This result concurs with most studies addressing this issue in multiple-episode BD patients (Barrera et al., 2013; Martino et al., 2011; Van Rheenen and Rossell, 2014) and contrasts with the well-documented impact of neurocognitive deficits on functional outcome in this illness (Burdick et al., 2010; Depp et al., 2012). This pattern is clearly at odds with findings reported in schizophrenia (SZ) where social cognitive deficits contribute to psychosocial deterioration beyond neurocognitive deficits (Pinkham and Penn, 2006). It is possible to hypothesize that some of these potential differences between schizophrenia and BD could contribute to understanding the dissimilarities in clinical picture and functional outcome seen in these disorders in everyday care practice.

Finally, some limitations of our results should be appraised. First, small sample size could have diminished our statistical power and true differences between groups could have gone undetected. Second, some studies suggested that social cognitive impairments might be accounted for neurocognitive deficits (Ioannidi et al., 2015; Martino et al., 2011). We controlled for neurocognitive variables when appropriate and differences between patients and healthy controls in cognitive ToM remained significant. However, a more complete subset of neurocognitive tools could have detected a more overt correlation between neurocognitive measures and social cognitive features, which could be the focus of future studies. Likewise, a more extensive evaluation of social cognition should be warranted in order to replicate our findings (i.e., extending these findings to emotional bias tasks) and to investigate whether gender imbalances could have affected the present result, in light of recent evidences suggesting an effect of gender in emotional processing tasks (Lungu et al., 2015). Furthermore, our sample size precluded us from detecting an influence of psychopharmacological treatment on such deficits, but future studies should address this influence as it was done extensively on neurocognitive (Donaldson et al., 2003; Wingo et al., 2009) and social cognitive domains (Martino et al., 2011). For instance, the well-established relationship between benzodiazepine use and fear recognition could have confounded our results. Finally, our sample was comprised only by patients with a psychotic manic episode and thus, results may not be readily generalizable to the entire population of BD patients.

5. Conclusions

In summary, BD type I patients recovered from their first manic episode exhibit an impaired ability to infer intentionality from others

(cognitive ToM) and a lower ability to recognize fear that were independent from neurocognitive performance. None of these performances were associated with psychosocial functioning. These findings suggest that the social cognition deficits reported in multiple-episode BD patients are already present at illness onset.

Conflict of interest

None.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Acknowledgement

None.

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