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ORIGINAL PAPER

Clinical and Cognitive Correlates of Insight in Bipolar Disorder

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Abstract
Insight is greatly impaired in Bipolar Disorder (BD), especially during mania. Cognitive impairment is also present in BD. Despite that, few studies have investigated a possible association between these two aspects. The main goal of the current study is to compare BD affective states regarding performance in cognitive testing and investigate clinical and cognitive predictors for insight loss in BD. The study investigated a sample of 65 patients who were evaluated in one of the BD phases (mania, euthymia or depression). All the subjects underwent neuropsychological evaluation and completed the Insight Scale for Affective Disorders (ISAD). The relationship between level of insight and clinical/cognitive variables was analyzed through multiple regression models. No significant differences were found among BD phases regarding performance on cognitive testing. Insight was more impaired in mania then in depression or euthymia. Predictors for loss of insight were: severity of manic symptoms and impairments in selective attention (Symbol search test), divided attention (Trail making test) and inhibition (Stroop test). The sample size is a potential limitation of the current study. Nevertheless, the results suggest this had limited impact, with group differences being detected for a number of variables. The results found have important clinical importance, suggesting, for example, that rehabilitation of specific cognitive skills may improve insight in BD.

Keywords Insight · Cognition · Bipolar disorder · Awareness

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Introduction

Insight is of great clinical relevance in the course of bipolar disorder. It has been shown that insight is frequently impaired in bipolar disorder (BD), especially in mania [25]. As indicated by a recent study, insight in BD is multidimensional, covering, for example, knowledge about having a condition or awareness of symptoms and functional changes [26]. Poor insight is associated with reduced treatment compliance and deterioration along the course of the disease [7]. A number of clinical characteristics have shown associations with insight, including level of manic and depressive symptomatology and illness duration, but the predictors may vary according to the phase of BD [25].

Cognitive changes in BD are relevant and clinically significant [5, 16]. They can affect attention, memory, learning and executive functions [12]. Some studies have compared BD phases regarding cognitive performance [14, 15, 27, 30]. In summary, these studies have found important impairments, with altered measures of executive functions and sustained attention among depressive bipolar and manic patients.

Several studies investigating the relationship between insight and cognitive changes have been conducted in neurological patients and later in patients with schizophrenia. Research with neurological patients, including individuals with dementia, has shown that cognitive impairment is associated with poor *insight* [2, 20]. Regarding patients with schizophrenia, it is unclear whether their lack of insight is more strongly associated with symptom severity or neuropsychological deficits [35]. The issue has been lately considered with respect to BD and correlations between lower levels of insight and higher impairment in executive function, verbal fluency and attention have been observed [9]. Attention has been addressed in only three studies that investigated its relationship with insight in BD. Braw et al. [4] found a significant correlation between poor insight and attention deficit, but Yen et al. [33] failed to find a relationship.

In summary, few studies have investigated the relationship between cognitive impairment in BD and loss of insight. Their findings show discrepancies and therefore demand further investigation. Accordingly, the objective of the present study is to compare BD mood phases in terms of performance in cognitive tests.

Materials and Methods

Participants and Setting

This study was performed in the BD outpatient research clinic in the Institute of Psychiatry of the Federal University of Rio de Janeiro (UFRJ), Brazil. The local Research Ethics Committee approved the study. All the patients in treatment in the outpatient clinic were invited to take part in the study. Those who accepted gave their written informed consent.

Inclusion criteria were: diagnosis of bipolar disorder type I or type II according to DSM-5 criteria [3] and age between 18 and 65 years. Exclusion criteria were: serious non-psychiatric disease (e.g. vascular disorder, organ failure) and fewer than 4 years of formal education.

The sample was comprised of 65 bipolar patients: 34 in euthymia, 11 in mania and 20 in depression phases. The study was performed between June, 2014 and February, 2015.

Instruments

Clinical and Demographic Variables

Socio-demographic data were collected as well as information on educational level, sex and age of each patient. A structured clinical interview according to DSM-5, was performed in order to establish a BD diagnosis. Patients were classified regarding their mood state – mania, depression or euthymia – according to DSM-5 criteria [3].

A psychiatric evaluation of each patient was performed by their physician through the following instruments: Young Mania Rating Scale (YMRS) [34] for manic symptoms, Hamilton Depression Scale (HAM-D17) [13] for depressive symptoms and the Clinical Global Impression, bipolar version (CGI-BP) [28] to assess bipolar disorder severity as a whole.

Insight Measure

The Insight Scale for Affective Disorders – ISAD – [22] was applied following translation and validation to Brazilian Portuguese [25]. Each item of ISAD is scored from 1 to 5, with 1 representing fully preserved insight and 5 indicating the most compromised insight. The ISAD-BR showed good internal consistency and good inter-rater reliability. A second order factor analysis indicated a hierarchical factor structure for the ISAD-BR, with four lower-order factors loading on a single higher-order factor [26].

Each physician was previously trained by the research coordinator with respect to the usage of the above-mentioned scales in order to ensure reliability. After the application of each scale, patients were individually submitted to cognitive evaluation by a neuropsychologist.

Cognitive Variables

The neuropsychological instruments were applied in a pre-established order for each patient. The testing took 30 min and evaluated several cognitive skills. The neuropsychological battery was comprised of: Digit Span (direct order and backwards), Letter-Number Sequencing and Search Symbol from the Wechsler Adult Intelligence Scale-Revised [32], The Stroop Color and Word Test (SCWT) [29], Trail Making Test Part A e B [11], and the verbal fluency test from Montreal Communication Evaluation Battery [10].

Statistical Analysis

Data analysis was carried out using SPSS software (version 20.0). Descriptive statistics were used to illustrate the sample characteristics. Differences in socio-demographic, cognitive variables and clinical characteristics according to mood state were tested with one-way ANOVAs, followed by pairwise comparisons with t-tests; for non-parametric variables, such as gender, the chi-square test was used as an alternative.

Differences in insight were explored with one-way ANOVAs, followed by post-hoc t-tests. These were calculated for total insight scores and also specifically for the first three items of the scale, concerning insight about having an illness and its consequences.

Stepwise regression models were calculated to investigate predictors of loss of insight in BD. To keep collinearity low, variables highly correlated with others (such as CGI score) were not included. For similar reasons, in the case of tests measuring related constructs (e.g. forward

and backward digit span), the most representative test for each cognitive function was chosen. In the case of some tests (e.g. TMT), summary measures were used. These procedures were also done to reduce the number of predictor variables in the regression models, considering the size of our sample.

The following variables were included: mania symptoms (YMRS total score), depression symptoms (HAM-D total score), semantic fluency (total number of clothes named in one minute), verbal working memory (backward digit span), attention and speed of processing (Symbol Search), task shifting ([Time taken to complete TMT Part B – Time taken to complete TMT Part A]/ Time taken to complete TMT Part A; following Netto and colleagues [21]), and inhibition (Stroop test; correct answers of the interference phase – correct answers of the color naming phase).

To avoid inflation of type II error and exclusion of predictors involved in suppressor effects, a backward regression method was used. In this procedure, all the predictors are initially included, and then one variable is deleted in each iteration considering the (lack of) contribution it gives to the model. This is done until no further improvement can be achieved by deleting predictors. The models were evaluated on the basis of the highest explained variance (R^2), highest cross-validity (adjusted R^2) and best Akaike's Information Criterion (AIC).

Results

Sample Characteristics

Clinical, cognitive and socio-demographic characteristics of the sample can be seen in Table 1. There were no significant group differences in terms of demographic variables or any cognitive test ($p > .05$). By contrast, as expected, there were significant differences in YMRS ($F(2, 62) = 60.92$, $p < .001$) and HAM-D scores ($F(2, 62) = 70.29$, $p < .001$), with higher scores in

Table 1 Socio-demographic, clinical and cognitive characteristics of participants

Variable	Euthymia ($n = 34$) Mean (SD) / Range	Mania (n = 11) Mean (SD) / Range	Depression ($n = 20$) Mean (SD) / Range	Group differences
Age	44.5 (9.6) / 29–64	46.5 (11.5) / 31–63	45.1 (12.1) / 19–63	–
Gender*	24/10	6/5	17/3	–
Years of education	11.0 (4.0) / 2–19	13.4 (4.2) / 4–17	12.6 (3.1) / 6–18	–
YMRS	1.3 (2.6) / 0–14	20.3 (10.3) / 8–41	4.3 (3.6) / 0–10	M > E = D
HAM-D	2.5 (2.3) / 0–8	4.3 (2.8) / 0–8	15.0 (5.8) / 4–25	D > E = M
CGI-BP global	1.3 (0.5) / 1–2	3.3(1.2)/ 1–7	4.0 (0.9) / 3–6	E < M = D
Digit Span				
Forward	6.9 (1.9) / 4–11	7.4 (2.1) / 4–11	6.8 (2.2) / 4–12	–
Backward	3.8 (2.5) / 1–13	3.5 (2.0) / 2–8	4.0 (1.7) / 2–9	–
Symbol search	22.1 (10.3) / 5–41	20.4 (10.1) / 6–41	21.6 (8.8) / 8–43	–
TMT**	1.3 (0.9) / -0.5–3.5	1.5 (1.1) / 0.4–4.3	1.3 (1.0) / -0.2–3.3	–
Stroop test***	−22.8 (13.9) / -47–27	−17.2 (8.0) / -31–-4	−15.6 (16.7) / -37–28	–
Phonemic fluency	18.0 (10.3) / 2–52	15.2 (9.2) / 5–37	15.0 (6.6) / 2–23	–
Semantic fluency	17.2 (7.5) / 5–43	14.0 (8.0) / 3–32	15.6 (5.0) / 7–26	–

*# Female/Male; YMRS – Young Mania Rating Scale; HAM-D – Hamilton Depression Rating Scale; CGI-BP– Clinical Global Impression scale–bipolar version; TMT – Trail making test

(Time taken to complete Part B – Time taken to complete Part A)/ Time taken to complete Part A); * (Correct answers of the interference phase – Correct answers of the color naming phase)

Table 2 Insight scores of participants

Variable	Euthymia ($n = 34$) Mean (SD) / Range	Mania ($n = 11$) Mean (SD) / Range	Depression (n = 20) Mean (SD) / Range	Group differences
ISAD item #1	1.7 (1.2), 1–5	2.0 (1.7), 1–5	1.3 (1.1), 1–5	–
ISAD item #2	1.1 (0.2), 1–2	2.2 (1.7), 1–5	1.2 (0.8), 1–4	E = D < M
ISAD item #3	1.7 (1.3), 1–5	2.4 (1.8), 1–5	1.3 (1.0), 1–5	–
ISAD total score	18.8 (2.4), 17–27	32.4 (12.8), 17–63	20.4 (4.3), 17–32	E = D < M

*ISAD- Insight Scale of Affective Disorders

YMRS during mania (p < .001) and in HAM-D during depression ($p < .001$). There was also a difference in CGI-BP scores (F (2, 62) = 79.52, $p < .001$), with less severity in euthymia in comparison with the other groups (p < .001).

Differences in Insight

Results can be seen in Table 2. There were significant group differences in total insight scores (F (2, 62) = 22.59, p < .001), with poorer insight in mania in relation to both euthymia and depression (p < .001). Exploring specifically the three first items of the scale, significant differences were found for item #2 ("Awareness of treatment efficacy for current symptoms or preventing relapses"); F (2, 62) = 7.58, $p = .001$), with patients in mania showing poorer insight than patients in euthymia (p = .001) or depression ($p = .013$). There were no significant group differences for ISAD items #1 ("Awareness of suffering from a affective disorder"); F (2, 62) = 1.06, $p = .353$) and #3 ("Awareness of consequences of the illness on work, family and social life"); F (2, 62) = 2.13, $p = .128$).

Regression Models

The regression models can be seen in Table 3. There was no evidence of collinearity in the data, with VIF and tolerance values within the recommended range (Field, 2013). All regression models significantly predicted insight in bipolar disorder (p < .001 in all models).

Table 3 Regression models with predictors for ISAD total scores

	Model 1		Model 2		Model 3		Model 4		Model 5	
Variable	β	p value	β	p value	β	p value	β	p value	β	p value
YMRS	.71	<.001	.71	<.001	.72	<.001	.74	<.001	.73	<.001
Symbol search	−.12	.181	−.13	.155	−.13	.153	−.18	.029	−.15	.060
TMT*	.13	.099	.13	.100	.13	.094	.13	.094	.13	.096
Stroop**	−.10	.244	−.11	.187	−.10	.221	−.11	.171		
Semantic fluency	−.17	.099	−.16	.108	−.11	.225				
Backward digit span	.11	.209	.11	.222						
HAM-D	−.04	.648								
Model p value	<.001		<.001		<.001		<.001		<.001	
R^2	.66		.66		.65		.64		.63	
Adjusted R^2	.62		.62		.62		.62		.61	

YMRS – Young Mania Rating Scale; HAM-D – Hamilton Depression Rating Scale; TMT – Trail making test

*(Time taken to complete Part B – Time taken to complete Part A)/ Time taken to complete Part A); ** (Correct answers of the interference phase – Correct answers of the color naming phase)

The models had high explained variance (R^2) and cross-validity (adjusted R^2), with minimal decreases in these values with the exclusion of variables. There was marginal improvement of the AIC in model 4, which included four predictors for compromised insight: severity of manic symptoms ($p < .001$), poorer performance in the Symbol Search ($p = .029$) and Stroop ($p = .171$), and longer time completing the TMT ($p = .094$).

Discussion

In this study, patients with BD were submitted to cognitive and insight evaluation with the aim of verifying if performance on the tests varied according to patient mood state as well as if there was a significant relationship between cognitive deficit and insight impairment. Patients in mania had poorer global insight and insight about treatment efficacy. No significant difference in cognitive performance was found when comparing mania, depression and euthymia. Regression models indicated that the best predictors for loss of insight in BD are severity of manic symptoms and cognitive performance in the TMT, Symbol search and Stroop test.

To the best of our knowledge, only four studies have so far compared BD mood states in relation to attention skills. In two of these studies, evaluating sustained attention, depressed patients had worse [30] or similar performance [14] when compared with bipolar patients in euthymia. In the two other studies, evaluating divided and selective attention [15, 27], depressed patients had better performance than those in mania. It is possible that no differences were found in the current study because of small subsamples for each BD phase. That is unlikely though, since effect sizes for differences in the cognitive tests were so low that very large samples would be needed to detect differences assuming similar effect sizes. A more likely explanation is that the severity of BD in the sample was mild, with reduced cognitive impairment in participants.

Regarding insight, the results in this study were similar to those of several others that found higher impairment in mania than in euthymia or depression [6, 24]. Furthermore, severity of manic symptomatology was a predictor of loss of insight in the regression models. In addition to the overall score, impairments during mania were found for insight about treatment efficacy. This highlights the potential effect of insight in treatment compliance, impacting on the prognosis of the illness [24].

It was also noted that impaired performance in Symbol Search, Stroop and TMT testing is related to poorer insight. Not many studies investigate the relationship between insight level and cognitive skills in BD. The association with the TMT confirms previous findings by Dias et al. [9]. To the best of our knowledge, no other study has indicated a relationship between performance in the Stroop and Symbol search tasks with insight into BD. These three tasks have in common the measurement of executive functions, which are thought to give an important contribution for awareness [1]. Models of awareness have suggested that mechanisms based on executive functions are essential for the monitoring of performance, including detection and response to errors [20]. Frontal lobe dysfunction has been proposed as an important pathological mechanism in BD, and it has been suggested that prefrontal cortex [18] and frontoparietal dysfunction [9, 31] *are related to poor insight in BD.*

It is notable that in terms of the specific abilities measured by these tasks, attention, cognitive flexibility and inhibition feature prominently. This may suggest that patients during mania have poor abilities to appropriately select and encode information about their condition. Some authors suggest that there is no difference between attention and awareness, with both corresponding to the same cognitive phenomenon [8, 17, 19, 23]. In addition, impairments in

cognitive flexibility may indicate poor ability to incorporate new information, discrepant with previous self-knowledge. Altogether, these would lead to a distorted sense of self ability, with personal information about ability being compromised [20].

Limitations

This study was conducted with outpatients in a University Hospital, therefore limiting the illness severity of the sample and introducing sampling biases. Another potential limitation of the current study refers to the sample size. However, the results suggest that sample size had limited impact, with group differences being detected for a number of variables; nevertheless, considering the sample size, controlling for medication was not possible. In addition, the regression models were robust, explaining a very high proportion of variance in insight.

Conclusion

The results in this study show that insight is worse in the manic phase and that there is a correlation between lower levels of insight and higher impairment in performance of attention, inhibition and cognitive flexibility testing. Identifying such predictors allows planning cognitive rehabilitation so as to target insight improvement, leading to better treatment compliance and prognosis.

Compliance with Ethical Standards

Conflict of Interest Evelyn Camelo declares that she has no conflict of interest.
Daniel Mograbi declares that he has no conflict of interest.
Rafael de Assis da Silva declares that he has no conflict of interest.
Cristina M. T. Santana declares that she has no conflict of interest.
Rodrigo L. Ferreira do Nascimento declares that he has no conflict of interest.
Adriana Cardoso de Oliveira e Silva declares that she has no conflict of interest.
Antônio Egídio Nardi declares that he has no conflict of interest.
Elie Cheniaux declares that he has no conflict of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent Informed consent was obtained from all individual participants included in the study.

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