

Performance of Bipolar Disorder Patients in Attention Testing: Comparison with Normal Controls and Among Manic, Depressive, and Euthymic Phases

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Abstract Several studies on cognition in bipolar disorder (BD) have been developed on the last decade. Neuropsychological evaluation of attention in BD patients is fundamental since alterations in attention affect other cognitive functions. Evaluate if performance of BD patients in attention tests varies according to each phase of the disease and verify if there are differences in attention when comparing BD patients with normal controls. The study included 101 BD patients, with ages between 18 and 65 years, being 52 euthymic, 22 manic and 27 depressive, besides 30 normal controls. All subjects were evaluated through Hamilton Depression Scale, Young Mania Rating Scale and Global Assessment of Functioning, bipolar version (CGI-BP). Attention was evaluated through a neuropsychological battery. Normal controls had a better performance in selective attention tests than BD patients. No differences were found among manic, depressive and euthymic phases. Attention is markedly impaired in BD. Nevertheless, the results of this study do not imply that the severity of the attention deficit in BD patients varies according to disease phase.

Keywords Attention · Bipolar disorder · Cognition · Mania · Depression · Euthymia

Introduction

Bipolar disorder (BD) is associated to significant cognitive impairment observed not only in manic and depression phases, but also in euthymia [31, 35]. In BD, changes in attention are relevant since impairment in attention may affect the remaining cognitive functions—memory, learning and executive functions [13].

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Over 100 studies have compared BD patients with normal controls or subjects with other mental disorders regarding performance in attention testing [4]. Attention is usually less impaired in BD than in schizophrenia but more affected in unipolar depression than in normal controls [4]. However, such studies usually do not discriminate the disorder phase affecting the patient at the moment the evaluation [2, 3, 5]. Performance in attention tests seems to be worse in manic phases. Nevertheless, few studies have compared bipolar patients in different mood states [16, 18, 26, 28].

This study aims at evaluating if performance of BD patients in attention tests varies according to their mood state and if significant difference can be found when comparing performance of BD patients in attention tests with that of normal controls.

Materials and Methods

Participants and Setting

This study was performed in the bipolar disorder outpatient research clinic in the Institute of Psychiatry of the Federal University of Rio de Janeiro (Instituto de Psiquiatria da Universidade Federal do Rio de Janeiro - UFRJ), Brazil. The local 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.

Socioeconomic data were collected as well as information on educational level, sex and age of each patient [6]. Inclusion criteria were: diagnosis of bipolar disorder type I or type II according to DSM-IV-TR criteria [1] and age between 18 and 65 years. Exclusion criteria were: serious non-psychiatric disease and refusal to give written informed consent.

The sample was composed of 101 bipolar patients: 52 in euthymia, 22 in mania and 27 in depression. Thirty (30) normal controls, employees of the Institute of Psychiatry of UFRJ, were also evaluated. The study took place between January, 2013 and December, 2014.

Instruments

Psychiatric Evaluation

A structured clinical interview according to DSM-IV-TR axis, SCID-I, I was performed in order to establish a BD diagnosis [8]. Patients were classified regarding their mood state—mania, depression or euthymia—according to DSM-IV-TR criteria [1].

A psychiatric evaluation of each patient was performed by their physician through the following instruments: Young Mania Rating Scale (YMRS) [38] for manic symptoms, Hamilton Depression Scale (HAM-D17) [14] for depressive symptoms and the Clinical Global Impressions Scale-bipolar version (CGI-BP) [29] to assess bipolar disorder as a whole. Each physician was previously trained by the research coordinator (EC) regarding the usage of the above-mentioned scales in order to ensure reliability.

Neuropsychological Tests

After the application of the psychiatric scales, patients went through a neuropsychological evaluation by a neuropsychologist who was not aware of the patients' mood states. The

normal controls were submitted to the same evaluation. The neuropsychological instruments were applied in a pre-established pattern for each patient. The testing lasted approximately 30 min and evaluated selective and divided attention. Initially a socio-demographic questionnaire was applied. Next a neuropsychological battery was used to evaluate selective attention. It included the following instruments: *Digit Span* (direct and reverse orders), Wechsler Adult Intelligence Scale-Revised (WAIS-III) [22, 35]; *Letter–Number Sequencing*, part of Wechsler Adult Intelligence Scale [36]; *The Stroop Color and Word Test (SCWT)* [30]; and *Search Symbol*, part of Wechsler Adult Intelligence Scale [35, 36]. *Trail Making Test Part A e B (TMT-A e B)* were used to evaluate divided attention [12]. The Verbal Fluency Test, part of the Montreal Communication Evaluation Battery (MAC, in BRAZIL) was used to evaluate the executive functions [9] in order to clarify whether attention problems possibly found could derive from executive function impairment.

Attention performance was tested in BD patients against the same testing in normal controls. Besides, a comparison among mania, depression and euthymia in those patients was also performed.

Statistical Analysis

Data analysis was carried out using SPSS software (version 20.0) [23]. Descriptive statistics were used to illustrate the sample characteristics. Differences in socio-demographic and clinical characteristics according to mood state were tested with one-way ANOVAs, followed by pairwise comparisons with t-tests; for non-parametric variables Chi square or Kruskal–Wallis tests were used as an alternative. For clinical characteristics, the comparisons were restricted to BD patients.

A similar approach was used to explore differences in cognitive tests between patient groups, with one-way ANOVAs comparing the four groups being followed by pairwise comparisons with t-tests. To control for the effect of multiple testing, Bonferroni corrections were used. In order to reduce the number of tests, summary measures were used in the case of some tests. Specifically, summary scores were used for the TMT ((Time taken to complete Part B – Time taken to complete Part A)/Time taken to complete Part A), and for the Stroop test (Correct answers of the interference phase – Correct answers of the color naming phase).

Results

Sample Characteristics

Clinical and socio-demographic characteristics of the sample can be seen in Table 1. There were no significant group differences in terms of demographic variables ($p > .05$). By contrast, as expected, there were significant differences in YMRS ($F(2, 98) = 70.71$, $p < .001$) and HAM-D scores ($F(2, 98) = 105.36$, $p < .001$), with higher scores in YMRS during mania ($p < .001$) and in HAM-D during depression ($p < .001$). There was also a difference in CGI-BP global scores ($F(2, 98) = 120.90$, $p < .001$), with less severity in euthymia in comparison with the other groups ($p < .001$), and higher severity in depression relative to mania ($p = .010$).

Table 1 Socio-demographic and clinical characteristics of participants

Variable	Euthymia (n = 52) Mean (SD)/range	Mania (n = 22) Mean (SD)/range	Depression (n = 27) Mean (SD)/range	Controls (n = 30) Mean (SD)/range	Group differences
Age	44.5 (10.5)/23–65	46.6 (10.9)/26–64	45.4 (12.2)/19–65	39.3 (13.4)/20–65	–
Gender*	36 (69.2)	14 (63.6)	23 (85.2)	18 (60.0)	–
Female	16 (30.8)	8 (36.4)	4 (14.8)	12 (40.0)	
Male					
Years of education	11.9 (4.3)/2–19	12.6 (3.5)/4–18	12.9 (3.1)/6–19	10.6 (3.4)/2–17	–
Socio-economic status**					
Low incon	13 (25.0)	3 (13.7)	5 (18.5)	8 (25)	–
Medium incon	30 (57.7)	14 (63.6)	20 (74.1)	17 (57.7)	
High incon	9 (17.3)	5 (22.7)	2 (7.4)	5 (17.3)	
YMRS	1.3 (2.4)/0–14	16.2 (9.2)/0–41	4.0 (3.6)/0–11	–	M > E = D
HAM-D	2.7 (2.4)/0–8	4.9 (3.9)/0–14	15.4 (5.4)/4–25	–	D > E = M
CGI global	1.3 (0.5)/1–2	3.3 (1.2)/1–7	4.0 (0.9)/3–6	–	D > M > E

YMRS Young Mania Rating Scale, HAM-D Hamilton Depression Rating Scale, CGI Clinical Global Impression scale

* # (%) Female/Male

** # (%) low/medium/high incon

Performance Differences in Cognitive Tests

Performance of participants in the cognitive tests can be seen in Table 2. There were no significant differences in performance between groups in the digit span (forward: ($F(3, 127) = 0.70$, $p = .555$), backward: ($F(3, 127) = 0.31$, $p = .818$)), TMT ($F(3, 127) = 0.70$, $p = .551$), Letter–Number Sequencing ($F(3, 127) = 0.54$, $p = .654$), phonemic ($F(3, 127) = 0.20$, $p = .894$) and semantic fluency ($F(3, 127) = 1.07$, $p = .367$). There were significant differences for the Stroop test ($F(3, 127) = 5.28$, $p = .002$) and Symbol Search test ($F(3, 127) = 4.18$, $p = .007$). Pairwise comparisons indicated that for the Stroop test, normal controls performed better than all 3 patient groups ($p < .05$), while in the Symbol Search test normal controls outperformed patients in mania only ($p = .005$).

Discussion

Since attention consists of a complex system associated with the activation of other cognitive functions, alterations in it jeopardize the remaining executive functions [20, 33]. In this study, bipolar patients in different phases were compared with normal controls regarding their performance in neuropsychological tests of attention. The objective was to verify if there is significant difference in attention performance between BD patients and normal subjects and among the different BD phases. Bipolar patients had worse performance than normal controls in two tests evaluating selective attention. More specifically, in one of the tests the difference was found only in manic patients. No significant difference was found in attention tests among BD phases.

Similarly to our results, several other studies found worse performance in tests of selective attention in BD patients in mania, depression and euthymia when compared with normal controls [4, 27]. Selective attention in BD patients is associated with structural and functional impairment in posterior and inferior parietal lobes [25, 26].

Regarding divided attention (digit span), a few studies [10, 11] besides this found no significant difference when comparing bipolar patients with normal controls. However, Rocca et al. [27] observed worse performance in tests of BD patients.

Not many studies have compared the performance on attention tests among the BD mood states. Three of them [17, 27, 32] found more severe attention impairment in mania and depression than in euthymia. However, two other studies [18, 19] found no significant differences when comparing euthymia, mania and depression, what is in accordance with the results in this study. It is possible that the sample size in this study has weakened the statistical power to detect differences among groups.

Cognitive impairment is one of the characteristics of the neuropsychological profiles of BD patients. Cognitive deficits may precede the disease [16, 24]. However, according to a few authors, such deficits get worse along time [15] and are associated with a higher number of affective episodes [34].

Therefore, the development of techniques of cognitive rehabilitation of BD patients are of utmost importance. A few studies [7, 21] have noted that it is possible to observe improvement in cognitive performance and psychosocial functioning in BD patients after just a few sessions of cognitive rehabilitation. Nevertheless, studies in the area are still too few.

Table 2 Cognitive performance of participants

Variable	Euthymia (n = 52) Mean (SD)/range	Mania (n = 22) Mean (SD)/range	Depression (n = 27) Mean (SD)/range	Controls (n = 30) Mean (SD)/range	Group differences
Digit Span					
Forward	7.2 (1.9)/4 to 12	7.0 (1.7)/4 to 11	7.2 (2.1)/4 to 12	6.6 (1.6)/4 to 10	–
Backward	4.0 (2.3)/1 to 13	3.5 (1.6)/2 to 8	3.8 (1.7)/1 to 9	3.7 (2.5)/0 to 14	–
Symbol search	22.5 (10.3)/2 to 41	19.0 (8.1)/6 to 41	22.1 (8.7)/8 to 43	27.6 (7.2)/10 to 43	C > M; M = D=E
TMT*	1.2 (0.8)/–.55 to 3.5	1.0 (1.1)/–.9 to 4.3	1.1 (0.9)/–.2 to 3.1	1.4 (1.0)/–.8 to 4	–
Stroop test**	–17.3 (19.1)/–47 to 36	–13.6 (15.2)/–33 to 23	–11.4 (19.0)/–37 to 32	–27.8 (11.0)/–45 to –8	C > E = M = D
Phonemic fluency	17.1 (10.6)/1 to 52	16.6 (8.2)/5 to 37	15.6 (6.7)/2 to 26	16.2 (5.8)/6 to 29	–
Semantic fluency	17.8 (8.0)/5 to 43	15.0 (8.2)/0 to 32	15.8 (5.1)/6 to 26	16.2 (5.0)/7 to 30	–
Letter–Number Sequencing	4.8 (3.0)/1 to 13	4.4 (2.4)/1 to 11	5.4 (2.8)/1 to 12	5.2 (7.2)/1 to 10	–

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

Conclusion

The results in this study show clear impairment in attention in BD, especially in selective attention. Conversely, it is unclear whether the severity of such impairment increases or decreases according to patients' mood states.

Conflict of interest Evelyn V. M. Camelo, Daniel Mograbi, Rafael de Assis da Silva, Jaqueline Bifano, Mayra Wainstok, Luciana Angélica Silva Silveira, Tânia Netto, Cristina M. T. Santana, and Elie Cheniaux declare that they have no conflict of interest.

Compliance with Ethical Standards

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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