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SHORT COMMUNICATION

The relationship between objective and subjective cognitive performance to clinical features in bipolar disorder: A 6 years follow-up study

Leticia Sanguinetti Czepielewski[a], Marcia Kauer-Sant'Anna[b,c], Flavio Kapczinski[c,d], Joana Bücker[e,*]

[a] *Programa de Pós-Graduação em Psicologia, Departamento de Psicologia do Desenvolvimento e da Personalidade, Instituto de Psicologia, Universidade Federal do Rio Grande do Sul (UFRGS), Porto Alegre, Brazil*
[b] *Department of Psychiatry, Federal University of Rio Grande do Sul (UFRGS), Porto Alegre, Brazil*
[c] *INCT of Translational Medicine, Brazil*
[d] *Department of Psychiatry and Behavioural Neurosciences, McMaster University, Hamilton, Canada*
[e] *Postgraduate Program in Medicine, Universidade do Vale do Taquari (UNIVATES), Lajeado, Brazil*

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Introduction

There is a consensus in the literature indicating that patients with Bipolar Disorder (BD) show cognitive impairments, especially in executive function, during both acute episodes and euthymia.[1] An emerging body of knowledge indicates the importance of promoting functional recovery and improving cognitive deficits to achieve an adequate treatment of BD. However, the trajectories of cognitive deficits are still unclear. The neuroprogression hypothesis suggests that BD may present a progressive course with cognitive and functioning decline, which may be associated with mood episodes, length of the illness, early trauma,[2] and biological rhythms disturbance, which may be a feature of BD.[3] However, most of the evidence in this field came from cross-sectional studies, and the few existing longitudinal studies bring contrary results.[4] A small number of studies assess the patient's perception of their cognitive function, which might be highly relevant to their everyday life.[5] Therefore, the ideal study to assess the progression of cognition in BD might include objective as well as subjective measures from a longitudinal perspective.

Thus, the purpose of the present study was to evaluate longitudinal cognitive performance in a sample of individuals with BD at baseline and after six years. All patients were in a depressive episode at baseline and euthymic at follow-up. We assessed subjective and objective cognitive difficulties in both points. We also investigated the relationship between psychosocial functioning, biological rhythms, and childhood trauma to cognition and the course of the illness. As far as we know, this is the first report using specific instruments to measure the relationship between these aspects to objective and subjective cognitive difficulties in a longitudinal BD sample.

Methods

Participants comprised 11 individuals that followed psychiatric treatment during the study at specialized outpatient clinics of the Hospital de Clinicas de Porto Alegre, Rio Grande do Sul, Brazil. Data collection was from two different projects approved by the local ethics' committee[5,6] (Project 15-0298) and (Project 08-145), with a mean time of

* Corresponding author at: Av. Avelino Talini, 171 - Universitário, Lajeado, RS, 95914-014.
E-mail address: joana.bucker@univates.br (J. Bücker).

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Table 1 Participants characteristics at baseline and after 6 years.

Variable	T1	T2
Hamilton Depression Rating Scale (HAM-D)	21.18 (±6.40)	3.91 (±1.22)
Young Mania Rating Scale (YMRS)	0.82 (±1.17)	0.64 (±0.81)
Biological Rhythm Interview Assessment in Neuropsychiatry (BRAIN)	54.26 (±8.07)	34.30 (±11.07)
Functioning Assessment Short Test (FAST)	44.73 (±9.61)	30.09 (±13.24)
Childhood trauma questionnaire (CTQ)	49.73 (±26.48)	64.67 (±10.26)
Letter-Number Sequencing WAIS-III subtest (SNL)	6.00 (±1.95)	7.55 (±4.11)
Cognitive Complaints in Bipolar Disorder Rating Assessment (COBRA)	27.82 (±8.82)	11.90 (±8.01)
Type of medication		
Lithium (%)	4 (36.3)	0
Anticonvulsants (%)	9 (81.8)	9 (81.8)
Antipsychotics (%)	6 (54.5)	8 (72.7)
Antidepressants (%)	3 (27.27)	1 (9)
Benzodiazepines (%)	7 (63.63)	4 (36.3)

*Values are presented as mean (standard deviation) unless indicated otherwise.

6,38 years between assessments. Research was conducted in accordance with the Helsinki Declaration. After a complete verbal description of both studies, all participants provided written informed consent. Evaluations at both times included sociodemographic, pharmacological data and clinical interview, which were administered by trained raters, in addition to the following instruments: Biological Rhythm Interview Assessment in Neuropsychiatry (BRIAN),[7] the Functioning Assessment Short Test (FAST),[8] Childhood trauma questionnaire (CTQ),[9] Hamilton Depression Rating Scale (HAM-D)[10] and Young Mania Rating Scale (YMRS)[11] (manic and depressive symptoms), and vocabulary and matrix reasoning subtests from Wechsler Abbreviated Scale of Intelligence (WASI)[12] (estimated IQ). Objective cognition was assessed by the Letter-Number Sequencing subtest of the WAIS-III[13] and subjective cognition was by Cognitive Complaints in Bipolar Disorder Rating Assessment (COBRA).[14] We performed our analyses in R (version 4.0.0) and RStudio (version 1.3.959). We tested the effects of time through linear mixed-effects models with restricted maximum likelihood (REML), including objective and subjective cognitive performance as the dependent variables, the evaluation time (T1/T2) as fixed effects, and a random effect for participants. We tested additional models with interaction terms between time of the assessment and biological rhythms, functional outcome, and childhood trauma.

Results

At first assessment, participants had 46.18 (±5.51) years old, 10.27 (±3.69) years of education, 25.73 (±11.36) years of illness duration, 20.45 (±8.74) years at illness onset, 2.73 (±4.38) number of suicidal attempts, 2.50 (±2.32) number of hospitalizations, 36.56 (±36.31) number of total mood episodes. 9 were females and 2 were males, 9 individuals with BD I and 2 individuals with BD II and all patients were not employed. When we compared findings from both timepoints, participants improved their depressive symptoms (HAMD: $t(10) = -9.88$, $p < .001$), biological rhythms dysfunction (BRIAN: $t(9) = -5.56$, $p < .001$), and functional impairments (FAST: $t(10) = -2.967$, $p = .014$) at follow-up. No differences between times were found related to manic symptoms (YMRS: $t(10) = -0.559$, $p = .59$) and perceived childhood trauma (CTQ: $t(8) = 1.22$, $p = .26$) (Table 1).

We conducted a linear mixed-effects models that included random effects for participants, and time of assessment (T1 and T2) as categorical between-subjects fixed factor. The results indicated that patients showed a similar performance between times regarding objective cognitive difficulties (LNS: $t(10) = 1.62$, $p = .14$), but showed improvements in subjective cognitive complaints over time (COBRA: $t(9) = -5.54$, $p < .001$) (Fig. 1). Estimated IQ was independently related to objective ($t(8) = 2.49$, $p = .037$), but not subjective cognition ($t(8) = -1.08$, $p = .31$).

We did not find a time by depressive symptoms interaction in predicting objective ($t(7) = 1.72$, $p = .13$) or subjective cognitive difficulties ($t(7) = 1.26$, $p = .25$). Furthermore, there were no interactions between time and biological rhythms, functional outcome, and childhood trauma for both objective and subjective cognition ($p > .5$). There was a time by age interaction related to objective ($t(7) = -3.34$, $p = .01$), but not subjective cognition ($t(7) = 1.00$, $p = .35$).

Discussion

We found that individuals with BD had no difference in objective cognition over time, although they improved their performance on subjective cognition at follow-up. This gain was not directly related or moderated to depressive symptoms or other clinical variables independently, though the participants showed better functional outcomes and biological rhythms dysfunction. On the other hand, we found a discrepancy between objective and subjective cognitive trajectories, that was not entirely suggestive of a neuroprogressive trajectory of cognition. Interestingly, these findings might indicate that patients who follow psychiatric treatment may have protective effects of medication on cognition, even if they do not show any objective improvements,[2] in addition to having better regulation of biological rhythms[15] and psychosocial

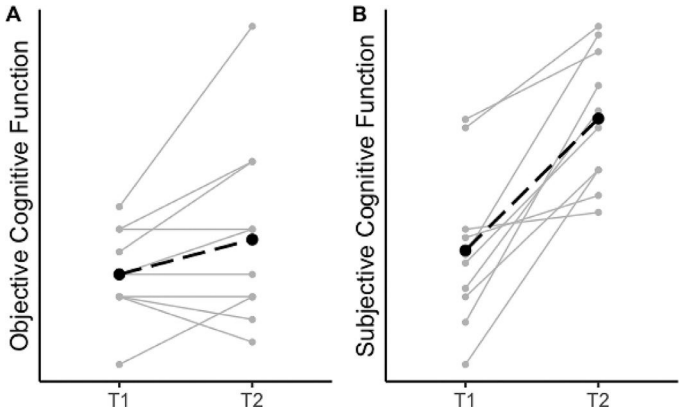

Fig. 1 Objective and subjective cognitive functioning at baseline and after 6 years.

higher functioning. Further, the improvement of depressive symptoms and the regulation of sleep and psychosocial functioning may influence patients' cognitive self-perception, which is highly relevant to their quality of life and well-being.[14] Therefore, in our patients with BD following psychiatric treatment, even though we did not find evidence of improvement in objective cognition — which was more related to estimated IQ and age, we found that over time these individuals reported perceiving better their cognitive function — which may be more related to a dimension of psychosocial functioning.

Our results must be interpreted in light of limitations. First, it is a small sample size that could reduce the power to generalize results and did not allow us to discuss the relationship between subjective cognitive performance and sociodemographic characteristics. Nonetheless, it is a prospective follow- up of 6 years, which is difficult in this population that is characterized by non-adherence to health care. Second, patients were not euthymic at first assessment, narrowing our findings because mood episodes might be related to neurocognitive decline. However, although ISBD Targeting Cognition Task Force recommend including partially or remitted patients in studies with cognition as a primary outcome, since subjective and objective cognition measures correlate poorly,[16,17] our results showed no time by depressive symptoms interaction in predicting objective or subjective cognitive difficulties. Third, we included only one objective neurocognitive test, while most researches have a more extensive battery. Notwithstanding these limitations, the present study shows the importance of evaluating both objective and subjective cognitive measures longitudinally. They bring different information regarding the cognitive function of individuals, in addition to psychosocial functioning and biological rhythms. Additionally, the clinical relevance of these results suggests that the improvement in self-reported cognition may be related to and help patients engage in adequate treatment and functioning in their everyday tasks. Future studies should follow these patients for an extended period (more than six years), in different stages of the disease, with a larger sample size, to evaluate the progression and the possible impact of adherence to treatment on BD's trajectory.

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Ethical considerations

Our study was conducted in accordance to the latest declaration of Helsinki. All participants signed a consent form, and the project was approved by the local ethics committee (Project 15-0298) and (Project 08-145).

Conflict of interest

The authors declare there are no conflicts of interest.

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