Pontifícia Universidade Católica
do Rio de Janeiro

Eduardo Fernandes Santos

Suicidality and disability in bipolar disorder

Dissertação de Mestrado

Dissertation presented to the Programa de Pós-graduação em Psicologia of PUC-Rio in partial fulfillment of the requirements for the degree of Master em Psicologia.

Advisor: Prof. Daniel Correa Mograbi

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ABSTRACT

Fernandes, Eduardo; Mograbi, Daniel Correa (Advisor); **Suicidality and disability in bipolar disorder**. Rio de Janeiro, 2023. 57p. Master's Dissertation – Department of Psychology, Pontifical Catholic University of Rio de Janeiro

The current work explores clinical predictors of disability and autobiographical memory episodic specificity in bipolar disorder (BD). In addition, it investigates the relationship between disability and insight in this disease The results highlight the impact of depression and pervasive role of loss of insight in BD, indicating that it may also lead to increased disability and reinforces the association between depressive symptoms and disability, which has been consistently reported in literature. Additionally, the results of this study indicate that more severe symptoms of depression, higher level of suicidal ideation and lower illness severity act as predictors of impaired recall of specific autobiographical details in BD. Clinical predictors are frequently used in clinical practice to identify patients at risk of adverse outcomes. Therefore, this research aimed at contributing to advance the understanding of the disease with direct relevance for clinical assessment and possible interventions.

Keywords

Bipolar disorder; disability; insight; depression; autobiographical memory

RESUMO

Fernandes, Eduardo; Mograbi, Daniel Correa; **Suicídio e incapacidade no transtorno bipolar**. Rio de Janeiro, 2023. 57p. Dissertação de mestrado – Departamento de Psicologia, Pontifícia Universidade Católica do Rio de Janeiro

O presente trabalho investiga preditores clínicos de incapacidade e especificidade episódica da memória autobiográfica no Transtorno Bipolar (TB). Além disso, investiga a relação entre incapacidade e insight nesses indivíduos. Os resultados destacam o impacto da depressão e o papel generalizado da perda de insight no TB, indicando que o insight pode levar ao aumento da incapacidade e reforça a associação entre sintomas depressivos e incapacidade, o que tem sido consistentemente relatado na literatura. Além disso, os resultados deste estudo indicam que sintomas mais graves de depressão, maior nível de ideação suicida e menor gravidade da doença atuam como preditores de prejuízos na habilidade de recordação de detalhes autobiográficos no TB. Preditores clínicos são frequentemente usados na prática clínica para identificar pacientes em risco de resultados adversos. Portanto, esta pesquisa visa contribuir para o avanço da compreensão da doença com relevância direta para avaliação clínica e possíveis intervenções.

Palavras-chave

Transtorno bipolar, incapacidade, insight, depressão, memoria autobiográfica

TABLE OF CONTENTS

1 **THEORETICAL BACKGROUND**

1.1 BIPOLAR DISORDER

Bipolar disorder (BD) is a complex, chronic and recurrent clinical condition characterized by depressive and manic/hypomanic episodes, with mood episodes alternated with periods of symptomatic remission (American Psychiatric Association, 2022). It affects 1–2% of the population worldwide (Clemente et al., 2015), reaching 5% when including subsyndromal forms (Merikangas et al., 2011). Since no biomarker has yet been approved for diagnosis of any mental disorder, clinical criteria for BD endure (Grande et al., 2016), including those from the International Classification of Diseases (ICD) or the Diagnostic and Statistical Manual of Mental Disorders (DSM), in addition to clinical performance-based guidelines (Hu et al., 2023).

BD is subdivided in DSM-5 TR (American Psychiatric Association, 2022) into two main types, type I (BD-I), type II (BD-II). In addition, other typified conditions include cyclothymic disorder, substance/medication-induced bipolar and related disorder, bipolar and related disorder due to another medical condition, other specified bipolar and related disorder, and unspecified bipolar and related disorder.

At least one manic episode must be presented for a diagnosis of BD-I in the DSM5-TR, although major depressive episodes are typical but not required for diagnosis. Whereas for BD-II, at least one hypomanic episode and one major depressive episode are required for diagnosis. Manic or hypomanic episodes are states of elevated mood and increased motor drive that are finite in time and differ in severity and length. Although a manic episode could impair social or occupational functioning and might encompass psychotic symptoms or even lead to hospital admission, a hypomanic episode does not typically cause severe impairment or require admission to hospital, yet a disturbance in functioning can be noticed by others (American Psychiatric Association, 2022)

1.2 SOCIAL IMPACT OF BIPOLAR DISORDER

1.2.1 **Suicide**

The incidence of death by suicide among patients with BD is high and can be more than 20 times higher than in the general population (Grande et al., 2016). In fact, suicidal behavior is quite frequent among subjects with BD, as up to 4–19% of them ultimately end their life by suicide, while 20–60% of them attempt suicide at least once in their lifetime (Dome et al., 2019). That is, one-tenth of BD patients die by suicide and this, coupled with an excess of mortality from natural causes, shortens average life expectancy by approximately 15 years (Harrison et al., 2018). Normally, suicide has not a single cause, but up to 90% of people who committed suicide meet the criteria for a psychiatric disorder, mostly mood disorders, substance use disorders or personality disorders (Rihmer, 2007).

Costa et. al (2014) reported through a systematic review on risk factors for suicide in BD that prolonged exposure to depressive episodes might increase the risk of suicide attempts in BD. In addition, BD-II has greater risk of suicide than BD-I patients and a possible explanation is that BD-II patients experience a predominantly depressive mood, mood lability, and mixed nature. Also, there is a strong association of predominant depression (especially with mixed episodes included) with suicidal behavior (Costa et al., 2015). Therefore, these results highlight the importance of early detection and treatment of psychiatric disorders for the prevention of suicidal behavior in BD.

1.2.2 **Disease Burden**

High-quality data on the epidemiology of BD as well as other mental illnesses are essential for formulating mental health policy and delivery of appropriate care services (Nuri et al., 2018). In addition to epidemiological data, health and social policies need to be provided with complete and current information about the health impacts of BD in comparison to other diseases and injuries, and for this, the burden of disease estimates is an important metric (Ferrari et al., 2016). Individuals with BD have high rates of psychiatric and

medical comorbidity, which contributes to increased utilization of healthcare resources (Sajatovic, 2005). A study showed that treatment to prevent the recurrence of BD episodes is the most effective way to reduce costs (Dean et al., 2004)

Da Silva et al. (2021) reported an analysis of official data obtained from the Citizen Information Service of the National Social Security Institute (SIC INSS) regarding sick leave and ill-health pensions in Brazil from January to November 2020 and they showed that mental illness was the fourth leading cause of ill health retirement and the third leading cause of temporary sick leave. The authors also analyzed official data provided by the Unified Benefits Information System *(Sistema Único de Informações de Benefícios, SUIBE)* regarding all active benefits paid to people with mental disorders. Results showed that there were 65,453 employees temporarily off work due to mental illness, which represent around 8% of all sick-leave benefits paid.

Studies have shown that BD patients have high occupational impairment with low role performance following recovery from an episode (Dean et al., 2004). Morselli et. al. (2004) reported in a cross-national analysis of unemployment that less than 50% of the BD population declared to have an active job. For each nation, the percentage of unemployed in the BD group (age range: 46–58 years) is significantly above the mean level of unemployment in each of those respective countries (Morselli et al., 2004).

BD is associated with a greater degree of disability than several prominent chronic medical conditions, including osteoarthritis, human immunodeficiency virus infection, diabetes, and asthma (Sajatovic, 2005). This result demonstrate that BD presents great functional impairment, with the support of public policies playing an essential role in the treatment of the disease, as well as in promoting a better quality of life for these patients.

1.2.3 **Disability**

Disability is a state of decreased functioning associated with disease, disorder, injury, or other health conditions, which in the context of one's environment is experienced as an impairment, activity limitation, or participation restriction (Tuomilehto & Wareham, 2006). In a review, Sanchez-Moreno et al., (2009) reported that a high percentage of bipolar patients (30-60%) showed significant disability in different areas of functioning, including social, work and family life. The authors concluded that several factors are associated with low functioning and disability, with the most frequent among clinical factors being persistent subsyndromal symptoms and the neuro-cognitive factors, considered as having a negative impact on the functional outcome.

According to the World Health Organization (WHO), BD was considered the 6th leading cause of disability in the world (WHO, 2011). In addition, it is usually linked to Disability-adjusted life years (DALYs) (He et al., 2020). According to WHO (2013), DALYs represent a societal measure of the disease or disability burden and it can be calculated by combining measures of life expectancy as well as the adjusted quality of life during a burdensome disease or disability for a population (WHO, 2013). DALYs are related to the quality-adjusted life year (QALY), which is complementary concepts. However, QALYs are years of healthy life lived and DALYs are years of healthy life lost (Arnesen & Nord, 2000). According to Ferrari et. al, 2016 DALYs is the most widely used and most representative evaluation and measurement indicator of the economic burden of disease.

1.3 CLINICAL CHARACTERISTICS

Significant developments in the scientific literature have been conducted by researchers to explore clinical characteristics of BD. For instance, there is evidence showing that BD patients have cognitive and neuropsychological impairments (Camelo et al., 2019; Martínez-Arán et al., 2004), higher emotion dysregulation problems, and higher impulsivity (Kulacaoglu & Izci, 2022), high co-occurrence with eating disorders (McElroy et al., 2005) and impairment in metacognition functioning (da Silva et al., 2020).

Therefore, efforts dedicated to the study of BD and its characteristics are essential to understand the disease, as well as the development of interventions and treatment. To contribute to these findings, the current work investigated alterations in two self-concepts in this clinical population: Insight and the ability of autobiographical memory.

1.3.1 **Insight**

Accurate self-awareness is essential to choose activities according to our abilities and limitations and it plays a key role for optimal everyday functioning (Rosen et al., 2010). Impairment in self-awareness can be found in neurological and psychiatric conditions. The most used label in the neurological literature when referring to impaired self-awareness is termed anosognosia (Mograbi & Morris, 2018), which is a common feature of Alzheimer's disease (Mograbi et al., 2012), which may be a direct result of the disease process (Hannesdottir & Morris, 2007). When referring to clinical psychiatric conditions, the literature tends to use the term loss of insight to describe reduced awareness of morbid changes (Mograbi & Morris, 2018).

This term was first defined in 1934 as "a correct attitude to a morbid change in oneself'' (Lewis, 1934). In the DSM 5-TR, obsessive-compulsive disorders (OCD) have insight as the basis for specifiers. In this case, after clinical evaluation, the patient can have the insight considered good or fair insight, poor insight and with absent insight/delusional. In this latter case, the individual thinks OCD beliefs are probably true (American Psychiatric Association, 2022). Although the categorical classification of insight is clinically useful, some studies support a dimensional approach to understanding insight. For instance, David defined the concept of insight as having at least three distinct dimensions: recognition of the disease itself, the ability to recognize symptoms and compliance with treatment (David, 1990).

Insight in BD patients has been reported in several studies, including systematic reviews (Látalová, 2012; da Silva et al., 2014). The literature suggests that loss of insight in BD is related to the polarity of mood episode, with less

impairment in bipolar depression than in mania (da Silva et al., 2016; Lage et al., 2022). Also, there is a correlation between lower levels of insight and higher impairment in performance of attention, inhibition and cognitive flexibility testing. (Camelo et al., 2019).

1.3.2 **Autobiographical memory**

Autobiographical memory (AM) is the aspect of memory that is concerned with the recollection of personally experienced past events. It is central to human functioning, contributing to an individual's sense of self, to his or her ability to remain oriented in the world and to pursue goals effectively in the light of past problem-solving (Williams et al., 2007). In other terms, AM refers to our memory for specific episodes, episodic memory, and to our conceptual, generic, and schematic knowledge of our lives (Conway & Williams, 2008).

Tulving and Markowitsch (1998) distinguished the episodic component of autobiographical memory, which contains specific personal events situated in time and space, and the semantic component, which stores more general knowledge about a person's past (Tulving & Markowitsch, 1998). Conway (2001) identified three different levels of autobiographical memory retrieval, including periods of life, general events, and specific events (Conway, 2001). Impairment of autobiographical memory is often associated with difficulties in executive functions, such as metacognition, monitoring, and inhibitory control (Dalgleish et al., 2007)

Evan et. al (1992) reported that patients with a history of parasuicide produced significantly more over general memories than a control group. In this case, this phenomenon occurred significantly more in response to positive cues and that latency to first responses was significantly delayed within the parasuicide group. Furthermore, the parasuicide group provided significantly fewer and less effective problem-solving strategies than the control group. (Evans et al., 1992).

Similarly, Williams and Broadbent (1986) showed that patients who attempted suicide by drug overdose generated fewer specific memories to cue

words compared to a group of patients with physical illness (Williams & Broadbent, 1986). The relationship of AM and over general recall tendency was observed in other mental disorders (e.g., major depressive disorder) (Brittlebank et al., 1993). This may occur to block emotional memories that have negative valence to avoid emotional turmoil associated with such memories (Williams, 1996).

Also, individuals diagnosed with BD can experience difficulties in the recall of specifically detailed autobiographical memories, tending to recall generalized descriptions rather than generate richly detailed accounts of events stored in memory (Mansell & Lam, 2004). De Assis et al. (2021) reported that depressed BD patients recall memories with fewer perceptual details and fragmented time integration, however, patients in mania generated memories with higher episodic detail, indicating this mood state may lead to more vivid re-experiencing. The authors suggest that as autobiographical memory represents the main source for patients to describe their past experience, its impairments may have an important impact on the clinical interview, as well as on the diagnosis of BD, with special attention to how memory details are generated across different mood states of the condition (da Silva et al., 2021).

2 **OBJECTIVES**

Based on the theoretical background presented above, the general objective of the present dissertation is to investigate suicidality and disability in bipolar disorder. For that purpose, two experimental studies were conducted, with the following specific objectives:

Study 1 – To investigate the relationship between loss of insight and disability in BD, exploring cognitive and clinical evaluation to investigate potential predictors of disability in BD;

Study 2 – To explore the relationship between clinical characteristics and autobiographical memory specificity in patients with BD, investigating the ability of patients diagnosed with BD to recall specific autobiographical details.

3 **ARTICLES SECTION**

Article 1

Fernandes, E.; Camelo, E., da Silva, R.; Netto, T; Cheniaux, E.; Mograbi, D (2023). Loss of insight and depression contribute to increased disability in bipolar disorder. (manuscript in preparation)

3.1 LOSS OF INSIGHT AND DEPRESSION CONTRIBUTE TO INCREASED DISABILITY IN BIPOLAR DISORDER

Abstract

Bipolar disorder (BD) may contribute to significant disability and reduced functioning in work, family and social life. This study investigates the relationship between loss of insight and disability in BD, exploring other potential predictors for the latter. A sample of 40 people with BD were recruited. All subjects answered an insight and disability scale and completed a clinical and neuropsychological evaluation. The relationship between disability, insight and clinical/cognitive variables was analyzed through correlations and multiple regression models. Total disability scores and social life disability were significantly associated with illness severity, depression and loss of insight, with the last two also being linked to family life disability. The regression model the best predicted disability in BD included depression and loss of insight. The results highlight the impact of depression and pervasive role of loss of insight in BD.

Keywords: Bipolar disorder; disability; insight; depression; self-awareness.

Introduction

Bipolar disorder is condition in which patients experience, during the course of the illness, fluctuating levels of severity of manic and depressive symptoms interspersed with euthymic periods (Judd et al., 2005). It affects more than 1% of the world's population, with up to 4% if a bipolar spectrum is considered (Grande et al., 2016; Akiskal & Pinto, 1999). Increasing evidence suggests that BD is associated with considerable burden (McIntyre & Calabrese, 2019). For instance, it has been found to be linked to increased suicidal behavior (Judd & Akiskal, 2003) and health care use/costs (Judd & Akiskal, 2003; Simon, 2003), higher unemployment (Coryell, 1993; Tse & Walsh, 2001) and dependence on public assistance (Judd & Akiskal, 2003), lower annual income (Goetzel et al., 2003), increased work absenteeism owing to illness (Simon, 2003; Goetzel et al., 2003; Hilty et al., 1999), decreased work productivity (Goetzel et al., 2003), poorer overall functioning (Goldberg et al., 1995; Pradhan et al., 1999) and lower quality of life (Simon, 2003; Vojta et al., 2001).

Disability is a state of decreased functioning associated with a disorder or other health condition, which in the context of one's environment is experienced as an impairment, activity limitation, or participation restriction (Altman, 2014). BD has been ranked as one of the leading medical causes of disability (WHO, 2011). Identifying the presence and severity of specific aspects of functional status in BD patients, and their correlation with demographic, clinical, treatment, environmental, and motivational variables, is important for understanding determinants of disability in specific disorders and states of illness (Harvey et al., 2010). Even during clinical remission, half of the patients with BD continue to experience difficulties in their functioning, with these dysfunctions potentially being related to several factors (Sanchez-Moreno et al., 2009). Previous studies explored factors related to disability in BD (Huxley & Baldessarini, 2007), but few investigated cognitive correlates (Camelo et al., 2019).

In the context of psychiatric disorders, the term insight refers to the capability of patients to recognize and accept that they are suffering from a mental illness (David, 1990). Loss of insight is an important feature of BD, particularly

during mania (da Silva et al., 2015; da Silva et al., 2015a; da Silva et al., 2016). Also, insight is of great clinical relevance in the evolution of BD, being more compromised during the phases of mania and mixed episodes than during depression and periods of euthymia (da Silva et al., 2015a), but with evidence suggesting that insight changes driven by mood are transient, with remission and no long-term effects during euthymia (da Silva et al., 2017).

Accurate self-awareness is essential for optimal everyday functioning, as it allows choosing activities that suit one's abilities and limitations (Johnson et al., 2002; Rosen et al., 2010) and, to the best of our knowledge, the relationship between loss of insight and disability has never been studied in BD. Additionally, most of the available studies that investigated disability in BD patients were conducted in developed countries (Sanchez-Moreno et al., 2009). Accordingly, this study aimed to investigate correlates of disability and loss of insight in BD patients from a Brazilian outpatient unit. Particularly, the study explored cognitive correlates and included a measure of insight of condition.

Methods

Sample

Forty patients with BD (19 in euthymia, 5 in mania and 16 in depression; DSM-5 criteria) were recruited in the outpatient unit of the Institute of Psychiatry of the Federal University of Rio de Janeiro (the project received ethics approval). Inclusion criteria were: diagnosis of bipolar disorder type I or type II according to DSM-5 criteria (APA, 2014) 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 study was approved by the local research ethics committee (CAAE: 36721320.0.0000.5263) and all participants provided informed consent.

Instruments

Demographic and clinical variables

Socio-demographic data (educational level, sex and age) were collected for all participants. Additionally, a structured clinical interview according to DSM-5 (APA, 2014) was performed in order to establish BD diagnosis. Assessment of clinical status included the following instruments: Young Mania Rating Scale (YMRS), an 11 items scale which assess manic symptoms (Young et al., 1978); Hamilton Depression Scale (HAM-D), a 17-item scale that evaluates the main depressive symptoms (Hamilton, 1960); the Clinical Global Impression, bipolar version (CGI-BP), a global score measuring the severity of the affective episode (Spearing et al., 1997); and the Positive and Negative Syndrome Scale – positive symptom subscale (PANSS-p), to detect the presence and intensity of psychotic symptoms as well as other positive symptoms (Chaves et al., 1998).

Insight

The Brazilian version of the Insight Scale for Affective Disorders (ISAD-BR; da Silva et al., 2015b) was used. The ISAD-BR showed good internal consistency and good inter-rater reliability. These psychometric results are similar to those obtained with the original scale (Olaya et al., 2012). Each item of ISAD is scored from 1 to 5, with 1 representing fully preserved insight and 5 indicating most compromised insight.

Disability

Disability was assessed using The Sheehan Disability Scale – SDS (Sheehan, 1996). The SDS is a 3-item self-rated scale of impairment, scale of measurement. The items address the impact of symptomatology on three areas of functioning: work, social and family. Participants qualify such limitations on visual analogical scales from 0 (no limitation) to 10 (maximum limitation).

Cognitive variables

A battery of tests was used to assess cognitive ability:

Digit span (Kaufman, 1983; Figueiredo & Nascimento, 2007) – This test requires the examiner to verbally present digits at a rate of one per second, measuring short-term memory and working memory.

Letter-Number Sequencing subtest from Wechsler Adult Intelligence Scale (WAIS; Kaufman, 1983; Nascimento & Figueiredo, 2002) – Participants are requested to listen to a string of alphanumeric characters and repeat the characters back verbally in a specific order, measuring working memory.

Search Symbol subtest from Wechsler Adult Intelligence Scale (WAIS; Kaufman, 1983; Nascimento & Figueiredo, 2002) – This is a self-paced task during which examinees are allotted two minutes to complete as many symbol discrimination items as possible. It was used to measures processing speed and visual perception.

The Stroop Color and Word Test (SCWT; Scarpina & Tagini, 2017; Repiso Campanholo et al., 2014) – The task was used to measure selective attention and cognitive flexibility. The person must speak the colors in which the words is printed, and not read the color name written.

Trail Making Test Part A and B (TMT-A and B; Lee & Chan, 2000; Repiso Campanholo et al., 2014) – In part A, the participant uses a pencil to connect a series of 25 encircled numbers in numerical order (measuring sustained attention); in part B, the participant connects 25 encircled numbers and letters in numerical and alphabetical order, alternating between the numbers and letters (measuring divided attention).

Statistical Analysis

Data analysis was carried out using SPSS software (version 28.0). Descriptive statistics were used to illustrate the sample characteristics. In order to identify which variables would be included in the models, initially Pearson correlations were calculated between SDS, cognitive, clinical and sociodemographic variables. Variables with significant correlations were included in stepwise multiple regression models investigating predictors of disability in BD. 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 (R2), highest cross-validity (adjusted R2) and best Akaike's Information Criterion (AIC). Considering the exploratory nature of the analyses, α was set at 0.05.

Results

Sample characteristics

The sample consisted of 32 women and 8 men, all diagnosed with BD type I and II. Clinical, cognitive and sociodemographic characteristics of the sample are presented in Table 1.

PLEASE INSERT TABLE 1 HERE

Correlations

Illness severity correlated with total SDS scores (r = .33, p = .037) and the social life disability subscale (r = .34, p = .031). Depressive symptoms correlated with total SDS scores (r = .42, p = .007), social life disability (r =.41, p = .007) and family life disability (r = .35, p = .028). Loss of insight correlated with total SDS scores (r = .48, p = .003), social life disability (r = .51, p = .001), family life disability (r = .37, p = .026) and showed a trend for a relationship with work disability (r = .31, p = .065). There were no significant correlations between disability and cognitive abilities or other clinical variables (p > .05).

Regression models

A multiple regression analysis with total SDS scores as the dependent variable and depressive symptoms, loss of insight and BD severity as predictors was calculated. Models can be seen in Table 2. The best model that significantly predicted (p = .001) disability in BD included depressive symptoms (standardized

β = .34, p = .033) and loss of insight (standardized β = .36, p = .022), with moderate explained variance (R2 = .33) and cross-validity (adjusted R2 = .29).

PLEASE INSERT TABLE 2 HERE

Discussion

In the present study, patients with BD underwent cognitive and clinical evaluation to investigate potential predictors of disability in BD. Results indicated that total disability scores and social life disability were significantly correlated with illness severity, depression and loss of insight. In addition, depression and loss of insight are also linked to family life disability. Regression models that best predicted disability in BD included depression and loss of insight.

Considering that most participants in the sample were euthymic patients, the association between illness severity and disability is consistent with previous findings (Perugi et al., 1988; Coryell, 1993) This suggests that recovery from a premorbid state after symptoms of mania or depression is expected, but that there is a significant social impairment even in the presence of complete remission of symptoms. These findings highlight the pervasive effects of BD, and its impact in everyday life.

The association between insight and disability is a novel finding. One potential explanation is that loss of insight may interfere with interpersonal relationships. Additionally, loss of insight impacts on treatment compliance (Sajatovic et al., 2009), which can also lead to increased disability. This is in line with previous findings indicating how impairments in insight can have important deleterious consequences for BD, for example being linked to increased suicidal ideation in bipolar depression (da Silva et al., 2017a). The relationship between loss of awareness and functional impairment has already been studied in other clinical populations, including those with schizophrenia (Lincoln et al., 2007) and Alzheimer's disease (Fischer et al., 2019).

Previous studies have reported that disability related to bipolar depression affects external and social aspects of patients' lives (Sanchez-Moreno et al., 2009). Depressive episodes are associated with greater impairment in work, family and social life than manic episodes (MacQueen et al., 2000; Özer et al., 2002). Considerable evidence indicates better insight in depression (da Silva et al., 2015), so the current findings suggest that the contribution of depression to disability happens despite increased insight.

The current study is one of the few to explore the role of cognitive factors in disability, a point which has been neglected in the literature, with most studies focusing on clinical variables (Sanchez-Moreno et al., 2009). Our findings did not indicate significant associations between cognitive abilities and disability, suggesting that other factors, such as affective state and self-awareness are more relevant predictors in BD. This suggests that other variables may be more robust predictors of disability, including insight about condition, which, to the best of our knowledge, was explored in relation to that theme for the first time in the literature.

This study has potential limitations. A first limitation refers to the sample size, particularly with a small number of patients in mania. In addition, considering the sample size, controlling for medication was not possible. Another potential limitation is that this study was conducted in an outpatient unit of a university hospital, introducing sampling biases. Nevertheless, this is a frequent limitation in the field of clinical studies. Therefore, studies with larger samples, conducted in different settings, are important to generalize the current findings.

Conclusions

The results highlight the pervasive role of loss of insight, indicating that it may also lead to increased disability, and an association between depressive symptoms and disability, which has been consistently reported in previous studies. Altogether, these results emphasize the need to manage these symptoms, even outside the acute stages of the illness, avoiding excessive disability in BD patients. Examples of potential intervention include

psychoeducation, which has been shown to improve illness outcomes (Colom et al., 2003; Scott & Colom, 2007). Therapeutic strategies that incorporate questionnaires and tasks to assess insight and disability in BD may enable interventions in these conditions and foster future research developments.

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Article 1:

Table 1 – Sample characteristics

Variable	Bipolar Disorder (n =40) Mean (SD) / Range
Age	45.1 (11.5) / 19-63
Sex*	32/8
Educational level**	11.9 (4.1) / 4-19
YMRS	3.9 (5.6) / 0–27
HAM-D	7.9 (7.1) / 0–25
CGI-BP global	2.6 (1.5) / 1–6
PANSS-p	8.2 (1.9) / 7-14
ISAD	9.7 (6.0) / 3–30
SDS	12.5 (8.9) / 0-30
MMSE	23.6 (3.8) / 14-30
Digital Span (forward)	6.8 (2.1) / 4-12
Digital Span (backward)	3.8 (1.9) / 2-9
Search Symbol	21.9 (10.2) / 5-43
STROOP	-18.7 (14.9) / -42-28
Trail Making (part A and B)	1.4 (0.9) / -28-3,27

*# Female/Male; ** # Years of education; YMRS – Young Mania Rating Scale; HAM-D – Hamilton Depression Rating Scale; CGI-BP– Clinical Global Impression scale–bipolar version; PANSS-p - Positive and Negative Syndrome Scale – positive symptom subscale; ISAD – Insight Scale for Affective Disorders; SDS - Sheehan Disability Scale; MMSE - Mini Mental State Examination

Article 2:

Table 2 – Predictors of disability in BD

	Model 1		Model 2	
Variable	β	p-value	β	p-value
ISAD	.37	.027	.36	.033
HAM-D	.34	.173	.34	.022
CGI-BP global	-.01	.971		
Model p-value	.005		.001	
R^2	.33		.33	
Adjusted R^2	.27		.29	
AIC	249.3		247.3	

ISAD – Insight Scale for Affective Disorders; HAM-D – Hamilton Depression Rating Scale; Scale CGI-BP– Clinical Global Impression scale–bipolar version

Article 2

Fernandes, E.; Lage, R.; da Silva, R.; Tancini, M.; Nascimento; Nardi, A.; Cheniaux, E., Mograbi, D. (2023). Clinical predictors of autobiographical memory episodic specificity in bipolar disorder (manuscript in preparation)

3.2 CLINICAL PREDICTORS OF AUTOBIOGRAPHICAL MEMORY EPISODIC SPECIFICITY IN BIPOLAR DISORDER

ABSTRACT

Autobiographical memory is essential for the assessment and diagnosis of psychiatric conditions, as well as for the formation of a sense of self and identity. However, very little is known about the relation between clinical variables and autobiographical memory, specifically in people with bipolar disorder (BD). **Objective:** To explore clinical predictors of the ability of patients diagnosed with BD to recall specific autobiographical details. **Methods:** This is a cross-sectional study that included sixty-three individuals with BD. Information regarding sociodemographic data and were collected, and the Hamilton Depression Scale, Young Mania Rating Scale, Clinical Global Impressions Scale for use in bipolar illness, Insight Scale for Affective Disorders, and the Beck Scale for Suicidal Ideation were administered. Additionally, patients responded with autobiographical memories to cue words belonging to four categories: mania, depression, BD, and neutral. Episodic specificity was scored according to the Autobiographical Interview, with high intra- and inter-rater reliability. **Results:** A higher level of suicidal ideation, more severe depressive symptoms, and lower illness severity significantly predicted reduced autobiographical memory specificity, with other variables not giving significant contributions. **Conclusion:** According to our results, more severe symptoms of depression, higher level of suicidal ideation and lower illness severity act as predictors of impaired recall of specific autobiographical details in BD. In contrast, level of insight does not seem to be able to predict episodic memory specificity in these individuals.

Keywords: Bipolar disorder; autobiographical memory; episodic memory; episodic specificity.

1. INTRODUCTION

Autobiographical memory can be defined as the ability to recall memories that are personally important and often emotionally charged[1]. This cognitive ability plays a critical role in everyday functioning, optimizing social interaction, ensuring the continuity of self/identity, and assisting in problem solving and implementation of appropriate behaviors[2]. The study of autobiographical memory can be particularly relevant for clinicians working with psychiatric conditions, given its importance for psychiatric anamnesis, interviews and self-reported measures.

A number of studies has indicated that autobiographical memory specificity is relatively reduced in individuals with depressed mood and major depressive disorder[3,4]. Clinically, it is possible to observe that patients with depression report overgeneral memories when attempting to retrieve specific events, for example reporting difficulties and feelings of sadness in the past without being able to provide specific details to anchor their vague memories[5]. Furthermore, it is known that with proper treatment, mood disorder patients can improve autobiographical memory specificity[4].

In bipolar disorder, an impairment in episodic memory is found even in euthymic individuals, probably due to difficulties organizing verbal information during encoding[6,7,8]. However, according to Sweeney et al.[9], depressed bipolar patients have cognitive impairments that are restricted to the domain of episodic memory, whereas bipolar patients in mixed/manic states of illness have widespread deficits across multiple cognitive domains. Also, the specificity of episodic memory can vary across different mood states, with patients in mania re-experiencing more autobiographical details than those in depression[10].

Moreover, other clinical factors can be linked to autobiographical memory specificity. For example, the study of Rohrer et al.[11] showed that patients with previous suicide attempts, with or without an affective disorder, had equally impaired autobiographical memory. Macdougall et al.[12] investigated the relationship between insight and episodic specificity in individuals with schizophrenia, and found that poorer recall of episodic details of negative events predicts impaired awareness of having a mental disorder in these patients.

However, very little is known about the relation between clinical variables and autobiographical memory specifically in people with bipolar disorder.

Thus, considering that autobiographical memory is essential for the assessment and diagnosis of psychiatric conditions, as well as for the formation of a sense of self and identity in patients, and given the relative scarcity of the literature on this topic, the current article investigates the relationship between autobiographical memory and BD. Specifically, this study aims to explore clinical predictors of the ability of patients diagnosed with BD to recall specific autobiographical details.

2. METHODS

2.1. Participants

This is a cross-sectional study, carried out at the BD outpatient clinic of the Institute of Psychiatry of the Federal University of Rio de Janeiro (IPUB-UFRJ). Inclusion criteria were diagnosis of type I or type II BD, being 18 years of age or older and having signed the informed consent form. Patients who did not accept to participate in the research, who did not cooperate in the application of the assessment instruments or who suffered from severe non-psychiatric illness were excluded. The study was approved by the IPUB-UFRJ research ethics committee (CAAE: 36721320.0.0000.5263).

2.2. Clinical Evaluation

Sociodemographic data (age, sex, and educational level) were collected. The diagnosis was formulated according to DSM 5 criteria[13] through a semi-structured interview, the SCID-5-RV[14]. The affective state of each patient was assessed by a trained psychiatrist, also according to the DSM 5 criteria. In each assessment, the following clinical scales were administered: Hamilton Depression Scale (HAM-D)[15], to assess depressive symptoms; Young Mania Rating Scale (YMRS)[16], for manic symptoms; Clinical Global Impressions Scale for use in bipolar illness (CGI-BP)[17], to assess the global severity of the current episode; Insight Scale for Affective Disorders (ISAD)[18], to estimate the level of insight; and Beck Scale for Suicidal Ideation (BSI)[19], to evaluate current suicidal

ideation and previous suicide attempts. Additionally, the presence of psychotic symptoms was also evaluated.

2.3. Autobiographical Memory

Patients were asked to remember the first autobiographical memory that came to mind after the interviewer said a cue word. The task used 12 words, divided into four three-word categories: mania (“aggressive,” “fast-talking,” “agitation”); depression (“demotivated,” “tired,” “depressed”); bipolar disease (“hospital,” “medication,” “hospitalization”); and neutral (“look,” “afternoon,” “stroll”). After the initial description of the memory, participants were asked when and where each memory happened. The interviews were recorded and fully transcribed for analysis. The scoring method used was based on the Autobiographical Interview, by Levine and collaborators[20]. Memories were classified according to the following details: time, place, perceptual, time integration, thought/emotion, and episodic richness, with each of these dimensions rated from 0 to 3, except for episodic richness—rated from 0 to 6, to provide a finer grained scoring[20]. That generated, for each cue word, total scores ranging from 0 to 21. Scores were summed across words and categories, yielding an overall memory episodicity score for each participant.

Intra-rater (test-retest) reliability was established by rating twice 10% of the material with a gap of 2 months between ratings. Average agreement was 75.5% (range: 57.3–87.5%) with an average Cohen’s kappa coefficient of 0.63 (range: 0.45–0.78; $p < .001$) indicating substantial agreement. Inter-rater reliability was assessed by a coder blind to group membership rating 10% of the material. Average agreement was 74.8% (range: 67.7–87.5%) with an average Cohen’s kappa coefficient of 0.61 (range: 0.55–0.78; $p < .001$) indicating substantial agreement.

2.4. Statistical Analyses

Data analysis was performed using SPSS software (version 26.0). Descriptive statistics were used to illustrate the characteristics of the sample, with groups separated according to affective state. Differences between these groups were tested with one-way ANOVAs, followed by post-hoc t tests, adjusted with

Bonferroni corrections, or chi-square tests, in the case of sex, education, presence of psychotic symptoms and previous suicide attempt.

Multiple linear stepwise regression models were calculated to explore the relationship of episodic memory specificity with clinical variables (depression [HAM-D], mania [YMRS], insight [ISAD], episode severity [CGI-BP], presence of psychotic symptoms, current suicidal ideation [BSI items #1-19] and suicide attempt history [BSI item #20]). The models were restricted to clinical variables because this was the main focus of the analysis, but also to avoid overfitting the model and having an excessive number of predictors in relation to observations in the sample. In all models, to avoid type II error inflation and the exclusion of predictors involved in suppressor effects, a backward regression method was used. The best models were selected based on a trade-off between the highest explained variance (R2), the highest cross-validity (adjusted R2) and the Akaike's Information Criterion (AIC).

3. RESULTS

3.1. Sample characteristics

A total of sixty-three patients with BD were evaluated. Of this total, 20 were in euthymia, 23 in depression and 20 in mania. In addition, 46 were women, 44 had no higher education, and only four had psychotic symptoms.

Sociodemographic and clinical characteristics of the sample can be seen in Table 1. As expected, there were significant differences between groups in HAM-D (higher scores in depression; $p < .001$), YMRS (higher scores in mania; $p < .001$) and CGI-BP scores (higher scores in mania and depression in relation to euthymia; $p < .001$). Significant differences were also observed for ISAD ($p < .001$), with patients in mania having higher scores than patients in euthymia and depression ($p < .001$), and the latter also having higher scores than the former ($p < .001$). The distribution of sex was marginally significant ($p = .044$), with more women in the mania group relative to the euthymia group ($p = .013$), but without any other significant differences.

There were no significant differences for age (p = .081), current suicidal ideation (p = .064), educational level (p = .395), presence of psychotic symptoms (p = .133) and previous suicide attempts (p = .851)

PLEASE INSERT TABLE 1 HERE

3.2. Regression models

There was no evidence of collinearity in the data, with VIF and tolerance values within the recommended range[21]. All regression models significantly predicted autobiographical episodic specificity. Table 2 shows the three models with best indexes.

PLEASE INSERT TABLE 2 HERE

Model 2 had the best trade-off considering best (lowest) AIC score, highest explained variance (R^2 = .26) and highest cross-validity (adjusted R^2 = .21), including depressive symptoms (HAM-D; standardized β = -.63, p = .001), illness severity (CGI-BP; standardized β = .77, p = .003) and current suicidal ideation (BSI-19; standardized β = -.29, p = .029) as predictors, with insight (ISAD; standardized β = -.21, p = .246) not giving a significant contribution to the model.

4. DISCUSSION

This study investigated the relationship between clinical characteristics and autobiographical memory specificity in patients with BD. According to our results, a higher level of suicidal ideation, more severe depressive symptoms, and lower illness severity significantly predicted reduced autobiographical memory specificity, with other variables not giving significant contributions.

According to the scientific literature, autobiographical memory is usually more generalized during depressive bipolar and depressive unipolar episodes[3,10,22]. Further, Da Silva et al.[10] studied episodic memory specificity in

different mood states of BD and found that depressed bipolar patients reported fewer details of perception and less time integration of memories than those in euthymia or mania. The results of the present study are in line with these findings, showing that bipolar patients with more severe depressive symptoms reported significantly fewer episodic details.

The relationship between autobiographical memory and suicidal behavior has been supported in the literature by several studies. A systematic review and meta-analyses conducted by Richard-Devantory et al.[23] showed that autobiographical memory was significantly less specific and more general in patients with a history of suicide attempt relative to those without such a history. Williams et al.[24,25,26] conducted some of the studies comparing episodic specificity of suicidal patients and non-depressed controls. The authors found that suicidal subjects' memory responses were more generic, and that they showed biases in the speed with which they could remember positive and negative events from their past due to delayed retrieval of positive memories. Some experts support that there is a relation between problem-solving and autobiographical memories specificity that intermediates the relation with suicidality, as a person faced with a problem would fail to access his or her past in order to generate possible solutions[27,28,29]. However, it is interesting to note that none of these studies have investigated current suicidal thoughts, with most authors analyzing only previous suicidal behavior. Furthermore, data specifically on the relation of suicidal thoughts in BD patients and episodic memory specificity are not yet found in the scientific literature. Despite that, our results follow those found in previous articles, with suicidal ideation acting as a significant predictor of less autobiographical details in BD.

In our sample, higher illness severity acted as a significant predictor of episodic memory specificity in BD. This result contradicts those in the literature that show that more severe depression is related to fewer episodic memory details[3,10,22]. However, it is important to notice that we had patients in different mood states in our sample, with 20 individuals in euthymia, 23 in depression, and 20 in mania. This might have influenced the results, since bipolar patients in

mania, that can also show high illness severity, generally re-experience more episodic details than those in depression[10].

Some limitations must be considered when interpreting the results of this study. The sample size precluded multivariate analysis of patients divided by each affective state. Furthermore, this study has a cross-sectional design, which is a limitation to infer causality. In addition, the fact that the study was carried out at a university hospital may have led to sampling biases. Another important limitation is that it was not possible to analyze the effect of medication on memory. It is well known that certain classes of drugs interfere with memory function (e.g., benzodiazepines[30]), and despite having most patients in the sample taking medication, the variety of types and dosages prevented us from analyzing these data. Therefore, future studies on autobiographical memory in BD in other settings and with larger samples are important to generalize current results, and to make possible categorizing patients according to medication status and explore predictors according to mood state.

The results of this study indicate that more severe symptoms of depression, higher level of suicidal ideation and lower illness severity act as predictors of impaired recall of specific autobiographical details in BD. In contrast, level of insight does not seem to be able to predict episodic memory specificity in these individuals. Current findings may help clinicians during the assessment of BD patients, especially when investigating past events that may be important to construct the course of the mental illness. Furthermore, the relationship between suicidal ideation and autobiographical memory details can be useful for the development of interventions aimed at reducing the suicide rate in this population.

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Article 2:

Table 1 – Socio-demographic and clinical characteristics of participants

Variable	Euthymia (n =20) Mean (SD) / Range	Mania (n = 20) Mean (SD) / Range	Depression (n = 23) Mean (SD) / Range	Group differences
Age	51.9 (12.1) / 33–79	53.8 (10.9) / 41–75	45.6 (13.1) / 23-70	–
Sex[1]	11/9	18/2	17/6	M>E
Educational level[2]	16/4	14/6	14/9	–
YMRS	1.4 (2.3) / 0–7	20.9 (7.0) / 13–40	2.1 (2.2) / 0–7	M>E=D
HAM-D	0.8 (1.7) / 0–7	3.6 (2.7) / 0–10	17.0 (5.7) / 8–28	D>E=M
CGI-BP global	1.1 (0.4) / 1–2	3.8 (0.9) / 3–6	4.0 (0.8) / 3–6	M=D>E
Psychotic symptoms[3]	20/0	17/3	22/1	–
ISAD	5.9 (3.9) / 3–14	29.7 (10.7) / 15–51	19.9 (5.6) / 9–31	M>D>E
Previous suicide attempt[4]	12/8	13/7	13/10	–
BSI-19	1.1 (3.4) / 0–12	3.2 (6.3) / 0–20	6.1 (9.2) / 0–29	–

1 # Female/Male; 2 # without/with further education; 3 # without/with psychotic symptoms; 4 # without/with previous attempt;
YMRS – Young Mania Rating Scale; HAM-D – Hamilton Depression Rating Scale; CGI-BP– Clinical Global Impression scale–bipolar version; ISAD – Insight Scale for Affective Disorders; BSI – Beck Scale of Suicide Ideation.

Article 2:

Table 2 – Regression models with clinical predictors for autobiographical episodic specificity

	Model 1		Model 2		Model 3	
Variable	β	p-value	β	p-value	β	p-value
HAM-D	-.71	.001	-.63	.001	-.52	.002
CGI-BP	.90	.002	.77	.003	.54	.001
BSI-19	-.30	.026	-.29	.029	-.25	.050
ISAD	-.26	.170	-.21	.246		
Psychotic symptoms	-.15	.256				
Model p-value	.002		.001		.001	
R^2	.27		.26		.24	
Adjusted R^2	.21		.21		.20	
AIC	568.5		567.9		567.4	

HAM-D – Hamilton Depression Rating Scale; CGI-BP– Clinical Global Impression scale–bipolar version; ISAD – Insight Scale for Affective Disorders; BSI – Beck Scale of Suicide Ideation.

GENERAL DISCUSSION

The general objective of this dissertation was to explore clinical predictors of disability and autobiographical memory episodic specificity in BD patients. In addition, investigated the relationship between disability and insight in these individuals. This research aimed at contributing to advance the understanding of the disease with direct relevance for clinical assessment and treatment.

In Article 1, both clinical and cognitive assessment were performed to investigate potential predictors of disability in BD. The Sheehan Disability Scale (SDS) was used to assess disability on three areas of functioning: work, social and family. In addition, we explored the relationship between loss of insight and disability. Our results showed that total disability scores and social life disability were significantly correlated with illness severity, depression and loss of insight, with the last two also being linked to family life disability. The study had a sample of 40 BD patients, most of them in euthymia. Therefore, the association between illness severity and disability is consistent with previous findings in the literature, suggesting that recovery from a premorbid state after symptoms of mania or depression is expected. However, there is a significant social impairment even in the presence of complete remission of symptoms. A multiple regression analysis was performed and demonstrated that the best model that significantly predicted disability in BD included depressive symptoms and loss of insight. Few studies have examined insight in BD (for a review: da Silva et al., 2014), showing frequently impairments, especially in mania (da Silva et al., 2015). Still, to the best of our knowledge, the relationship between loss of insight and disability has never been studied in this clinical condition, therefore the comparison with previous results is compromised. A previous review reported that most studies that explored disability in BD focused on clinical variables, neglecting the role of cognitive variables (Sanchez-Moreno et al., 2009). Our study explored both factors in the role of disability in BD showing no significant associations between cognitive abilities and disability and suggesting that other factors, such as affective state and self-awareness are more relevant predictors in BD. In this same review Sanchez-Moreno et al. (2009) reported that most of the available

studies that investigated disability in BD patients were conducted in developed countries. Accordingly, the results contribute to data regarding disability in BD in a developing country, which can be useful for formulating mental health policy and delivery of appropriate care services.

Article 2 investigated clinical predictors of autobiographical memory episodic specificity in BD. A total of sixty-three patients with BD (20 were in euthymia, 23 in depression and 20 in mania) were included. Clinical scales were administered and the patients were asked to remember the first autobiographical memory that came to mind after the interviewer said a cue word. The task used 12 words, divided into four categories: mania, depression, bipolar disorder and neutral with 3 words for each category. After the initial description of the memory, participants were asked when and where each memory happened. Episodic specificity was scored according to the Autobiographical Interview. A multiple regression analysis was performed in the study and demonstrated that higher level of suicidal ideation, more severe depressive symptoms, and lower illness severity significantly predicted reduced autobiographical memory specificity. In contrast, level of insight did not seem to be able to predict episodic memory specificity in these individuals. The relationship between suicidal ideation and depression symptoms showing an impact on autobiographical memory, precisely the ability of recall specific autobiographical details is in accordance with previous studies. In our sample, lower severity acted as a significant predictor of reduced episodic memory specificity in BD. This result contradicts those in the literature that show that more severe depression is related to fewer episodic memory details (Silva et al., 2021; Dalgleish et al., 2007). However, we had patients in different mood states in our sample, with fewer patients in mania, which might have influenced the results.

Clinical predictors are frequently used in clinical practice to identify patients who are at risk of developing an adverse outcome so that preventive measures can be initiated. Furthermore, they can play an essential role in assisting in clinical decision-making, treatment strategy and assisting healthcare services with planning and quality management (Chowdhury & Turin, 2020). Also,

clinical prediction models combine a number of characteristics (e.g., related to the patient, the disease, or treatment) to predict a diagnostic or prognostic outcome (Steyerberg, 2009). In the diagnostic work-up, the authors suggest that predictions can be useful to estimate the probability that a disease is present. When the probability is relatively high, treatment is indicated; if the probability is low, no treatment is indicated, and further diagnostic testing may be considered necessary.

Clinicians must understand the level of insight for each bipolar patient and consider the impacts of different clinical courses in BD on changes in insight (Yen et al., 2007). Limited awareness of having a disease, understanding of symptoms or their consequences can affect treatment adherence and significantly influence the course of the disease (Sajatovic et al., 2009). Therefore, the contribution of this work can help clinicians during the evaluation of patients with BD. In addition, these results emphasize the need to manage these symptoms, even outside the acute stages of the illness, avoiding excessive disability in BD patients. We recommend the development of therapeutic strategies that incorporate questionnaires and tasks to assess insight and disability in BD. Example of potential intervention include psychoeducation, which involves providing patients with information about BD and its treatment, with a primary goal being to improve adherence to pharmacological treatment by helping patients to understand the biological roots of the disorder and the rationale for pharmacological treatments (Colom & Vieta, 2006). In addition, patients are taught the early warning signs for episodes, and common triggers for symptoms, therefore, to investigate possible improvements in insight after psychoeducational intervention may contribute to the findings of this work, possibly allowing a better understanding of interventions in BD. On top of that, current findings may help clinicians during the assessment of BD patients, especially when investigating past events that may be important to construct the course of the mental illness. Furthermore, the relationship between suicidal ideation and autobiographical memory details can be useful for the development of interventions aimed at reducing the suicide rate in this population.

Some limitations must be considered when interpreting the results of this study. A first limitation refers to the sample size in both studies, especially with fewer patients in mania. Also, the sample size precluded multivariate analysis of patients divided by each affective state. Furthermore, this study has a cross-sectional design, which is a limitation to infer causality. In addition, the fact that both studies were carried out at a university hospital may have led to sampling biases. Nevertheless, this is a frequent limitation in the field of clinical studies. Another important limitation in Article 2 is that it was not possible to analyze the effect of medication on memory. It is well known that certain classes of drugs interfere with memory function (Crowe & Stranks, 2018), and despite having most patients in the sample taking medication, the variety of types and dosages prevented us from analyzing these data. Therefore, future studies on disability and autobiographical memory in BD in other settings and with larger samples are important to generalize current results, and to make possible to categorize patients according to medication status and to explore predictors according to mood state.

In summary, the current work highlights the impact of depression and pervasive role of loss of insight in BD, indicating that it may also lead to increased disability and reinforces the association between depressive symptoms and disability, which has been consistently reported literature. In addition, the results of this study indicate that more severe symptoms of depression, higher level of suicidal ideation and lower illness severity act as predictors of impaired recall of specific autobiographical details in BD.

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