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Original Article

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# Sexual function in patients with bipolar disorder type I evaluated in symptomatic remission: a cross-sectional study

Sexual function in bipolar disorder

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#### Abstract

**Introduction:** Bipolar disorder (BD) is a chronic pathology that is associated with several impairments throughout a patient's life, including decreased sexual function. Despite the importance in quality of life (QoL), functionality and medication adherence, it is still little investigated in these patients.

**Objective:** To compare the sexual function of patients with Bipolar Disorder type I (BD-I), in remission, with healthy controls (HC) and to investigate the clinical and socio-demographic characteristics associated with sexual function in these

individuals. Also, to assess the QoL in patients with and without sexual dysfunction (SD).

**Methods:** Cross-sectional study with 132 patients with BD-I in euthymic phase and 61 HCs from an outpatient clinic. All the participants were evaluated through the Arizona Sexual Scale (ASEX) and the brief version of the World Health Organization Quality of Life Assessment (WHOQoL-BREF). The patients with BD-I were compared with the HCs. The patients were divided into two groups: the ones diagnosed with SD and the ones without it.

**Results:** The patients with BD-I had higher rates of SD (42.4%) compared to the HCs (16.4%) (OR 3.67, 95% CI 1.55 – 8.67; p=0.003). SD in patients was associated with being women (p=0.001), older age (p=0.003) and having a longer duration of untreated illness (p=0.010). Patients with SD had worse QoL scores compared to those without SD.

**Conclusion:** Patients with BD-I have a high prevalence of SD and this was associated with worse QoL scores in all domains.

Keywords: bipolar disorder, sexual function, sexual dysfunction, quality of life.

#### Introduction

Bipolar disorder (BD) is a chronic pathology that affects approximately 2.4% of the world population<sup>1</sup>. Despite being controllable, it is associated with several impairments throughout a patient's life, including work capacity, interpersonal social relationships and Quality of Life (QoL). In this sense, although sexual function is one of the main factors associated with QoL, it is still little investigated in patients with bipolar illness<sup>23</sup>. Sexual dysfunction (SD) may lead to serious implication in patients with BD, as it further lowers their QoL and self-esteem, and impacts negatively on compliance with medication. Furthermore, most patients do not talk about their sexual problems with psychiatrists and few professionals ask questions related to the patients' sexual function<sup>4</sup>

It is important to remember that sexual function corresponds to the sexual response cycle and is comprised of three phases: desire/libido, arousal, and orgasm. SD occurs when there is difficulty in any of these phases of sexual response, or when there is pain during the sexual act <sup>56</sup>. SD has a multifactorial

background and may be related to side effects of medicines, anatomical, hormonal, psychic, behavioral and/or cultural issues, among other aspects <sup>7,8,9</sup>

Many studies that evaluated patients with BD neither used appropriate scales of measurement to assess sexual function, nor controlled the phase of the disorder, whether in crisis or in remission, among other factors<sup>10</sup>.Furthermore, there are several theories related to the presence of SD and most of them are associated to the use of medications, as well as the psychopathology of the mental disorder itself. In fact, psychotropic drugs act on various neurotransmission systems and hormonal axes involved in sexual function. One example is the increase in serotonergic activity with the use of antidepressants (ADs) and hyperprolactinemia resulting from the use of antipsychotics<sup>11</sup>

Given this scenario, the objectives of this study were: a. to investigate the clinical and socio-demographic characteristics associated with sexual function in bipolar disorder type I (BD-I), in symptomatic remission, and compare QoL between BD-I with and without SD. b. to compare the sexual function of patients with BD-I, with healthy controls (HCs).

#### Methodology

#### Study design, sampling, and participants

This cross-sectional study evaluated a convenience sample from an outpatient clinic in a Mood and Anxiety Disorders Program, located at a teaching Hospital at the Federal University of Bahia-Brazil. The sample was represented by BD-I patients and HC. All patients treated at the outpatient clinic were invited to participate in this study. The inclusion criteria were: people  $\geq$  18 years of age, diagnosed with BD-I according to the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I)<sup>12,13</sup>. The patients had to be in the euthymic phase by criteria that followed the recommendations of The International Society for Bipolar Disorders (ISBD)<sup>14</sup>: scores < 7 on the Hamilton Depression Rating Scale (HAM-D 17)<sup>15</sup> and Young Mania Rating Scale (YMRS)<sup>16,17</sup>, and absence of any acute episode at least in the past 8 weeks. We opted for stricter criteria of euthymia, in order to avoid interference from residual symptoms or mood-related answers. Also, they had to sign the Informed Consent Form (ICF). The exclusion criteria were the inability to understand or complete research instruments.

The HC group comprised volunteers from the same community who had

similar socio-demographic characteristics, such as family income, level of schooling and place of residence. They had been treated for other medical conditions at the outpatient center and a group of individuals in a similar number with regards to gender and age were selected. This was done in order to prevent bias associated with these variables. The exclusion criteria were: having any axis I mental disorder diagnosed through the SCID-I interviews; being unable to understand or complete research instruments; and refusing to sign the ICF.

#### Procedures

After assessing euthymia, the patients went through a semi-structured interview derived from the Brazilian Research Consortium for BD, containing clinical and socio-demographic characteristics, and they were interviewed through the SCID-I<sup>12,13</sup> and The Structured Clinical Interview for DSM-IV Axis II Disorders (SCID-II)<sup>18</sup>, to assess personality disorders. Afterwards, the participants were evaluated through the Arizona Sexual Scale (ASEX)<sup>19,20</sup> and the World Health Organization Quality of Life Assessment brief version (WHOQoL-BREF)<sup>21,22</sup>. The HC group was submitted to the same protocol. All participants were recruited during 2012-2019.

ASEX is a scale used to assess sexual function based on 5 questions that investigate: desire, arousal, penile erection/vaginal lubrication, ability to reach orgasm and orgasm satisfaction. Each item has a maximum score of 6 points, with higher scores suggesting higher SD level. SD is identified when there is a total score  $\geq$ 19, a score  $\geq$ 5 in one item or a score  $\geq$ 4 in 3 items <sup>19,20</sup>. In this study, in view of the gap in the literature regarding the sexual function of patients with BD, and in order to better understand the specific domains of sexual function, the items in the ASEX were separated. It was considered that a score  $\geq$  4 indicated impairment in the phase corresponding to the analyzed ASEX item, as can be seen in other studies in literature<sup>23–25</sup>

The WHOQoL-BREF is a scale that assesses QoL based on 4 domains: physical health, mental health, social relationships, and the environment. It is composed of 26 questions, the first two assessing the overall impression on both the individual's QoL (overall QoL) and general health. Each item can have a score from 1 to 5 and higher scores are associated with better QoL indices <sup>21,22</sup>. The

WHOQOL-BREF domains were continuously evaluated due to the lack of a welldefined cutoff point in the medical literature.

#### Ethics statement

All the instruments were validated for use in Brazilian populations. All procedures were approved by the ethics committee of the teaching Hospital and followed the guidelines in the Declaration of Helsinki/2013<sup>26</sup> and the Resolution 466/2012<sup>27</sup> on Human subject research of the Brazilian National Health Council. It was first approved by the ethics committee of the Federal University of Bahia Hospital in 2005, updated at *Plataforma Brazil* on September 14<sup>th</sup>, 2018 (protocol) 2.895.571) number and reapproved in 2021 (protocol number 86468818.7.1001.5577). All patients and HCs received information regarding the research and were evaluated by experienced and formally trained investigators (psychiatrists and psychologists). They were interviewed only after signing the ICF.

#### Statistical analysis

Data were added and analyzed in the Statistical Package for Social Sciences program in its 26.0 version (SPSS, Chicago, IL, USA) database. BD-I patients, after being divided into two groups: with and without SD, were compared to HC.

Categorical variables were described as absolute frequency (valid percentage) and compared using the Pearson's Chi-square test or the Mantel-Haenszel's Chi-square test for trend. Continuous variables were described as average (standard deviation) or median (interquartile interval), according to the assumption of normality assessed by skewness and kurtosis values, as well as graphical methods. For a greater clinical relevance, continuous variables were categorized for comparison purposes, based on previous studies or proportional sample distribution. Age was categorized into: 18-29 years, 30-49 years and  $\geq$  50 years<sup>28</sup>. Years of schooling were categorized as  $\leq$  9 years (elementary school), 10-12 years (high school) and >12 years (technical or higher education)<sup>28</sup> Age at the first episode was categorized as  $\leq$  18 years (early onset) and >18 years (late onset)<sup>29</sup>. The latency to the first treatment with a mood stabilizer was categorized as  $\leq$  5 years and > 5 years<sup>30</sup>. The progression time of the disease was

categorized into: 1-10 years, 11-20 years and > 20 years. The number of episodes throughout life was categorized: 1-5, 6-10 and > $10^{31}$ .

A binary logistic regression model was performed to assess the association between sociodemographic, clinical and SD variables (dependent variable) in patients with BD-I. A minimum relation of 5 events per variable was determined, and covariates with p<0.1 in the univariate analysis were taken to the final adjusted model. The medication profile (current use of lithium, AD, antipsychotics, and benzodiazepines) was included in the multivariate model regardless of the p-value due to clinical plausibility. Another binary logistic regression model was used to assess whether being a patient is more associated with the presence of SD (dependent variable) than HC when the depending variable is adjusted for sociodemographic and clinical factors. Covariates with p<0.1 in the univariate analysis were taken into the final adjusted model.

In both cases, the variables were tested for multicollinearity, and included in the regression in case the variance influence factor (VIF) was < 4. Missing data represented about 5% of the population of multivariate analyses and were disregarded. All tests were two-tailed and p-values <0.05 were considered significant at a 95% confidence interval.

#### Results

165 patients with BD-I were selected, of which 33 were excluded due to lack of data. Therefore, 132 patients were included. In the HC group 68 were submitted to the complete protocol, 7 being excluded due to lack of data. Therefore, 61 HC were assessed.

The mean age among patients was 42.1 ( $\pm$ 11.7); they had 12.6 ( $\pm$ 3.7) years of schooling, most being women (74.2%) aged between 30 and 49 years (56.8%), without a partner (61.4%), without paid occupation (68.7%), with at least one clinical comorbidity (63.6%) and in current use of mood stabilizer (96.9%) and antipsychotic (52.3%). At least one SD was identified in 56 (42.4%) patients (Table 1).

Variable		Sexual dysfunction		
	Total sample	Yes	No	_
	of BD-I	(n=56)	(n=76)	
			•	
				0.020a
18 20	10(14.4)	6 (10 7)	13 (17 1)	0.030
20.40	19 (14.4)	0(10.7)	15 (17.1)	
30-49	/5 (56.8)	28 (50)	47 (61.8)	
$\geq$ 50	38 (28.8)	22 (39.3)	16 (21.1)	
Female gender (yes)	98 (74.2)	50 (89.3)	48 (63.2)	0.001 <sup>b</sup>
with partner (yes)	51 (38.6)	22 (39.3)	29 (38.2)	0.895 <sup>b</sup>
Individual income (yes)	94 (71.8)	40 (71.4)	54 (72)	0.943 <sup>b</sup>
Religious affiliation (yes)	111 (84.1)	46 (82.1)	65 (85.5)	0.599 <sup>b</sup>
Paid occupation (yes)	41 (31.3)	9 (16.1)	32 (42.7)	$0.001^{b}$
Years of schooling		×		0.726 <sup>a</sup>
≤ 9	15 (12.1)	7 (13.7)	8 (11)	
10-12	47 (37.9)	19 (37.3)	28 (38.4)	
> 12	62 (50)	25 (49)	37 (50.7)	
Current smoking (yes)	42 (31.8)	19 (33.9)	23 (30.3)	0.655 <sup>b</sup>
Physical activity (yes)	39 (29.5)	14 (25)	25 (32.9)	0.326 <sup>b</sup>
Clinical comorbidity <sup>c</sup> (yes)	84 (63.6)	38 (67.9)	46 (60.5)	0.387 <sup>b</sup>
Age of onset				0.256 <sup>b</sup>
Early <mark>onset</mark> (≤18 years)	35 (26.5)	12 (21.4)	23 (30.3)	
Late onset (>18 years)	97 (73.5)	44 (78.6)	53 (69.7)	
Delay to first mood stabilize treatment (years)	er			0.010 <sup>b</sup>
$\leq 5$	75 (58 6)	24 (45 3)	51 (68)	0.010
> 5	53 (A1 A)	2 + (-5.5)	24(22)	
	55 (41.4)	<i>27</i> ( <i>3</i> 4. <i>1</i> )	24 (32)	

Table 1 – Clinical and sociodemographic characteristics of patients with BD-I with and without SD (N=132)

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Duration of illness (years)				0.033 <sup>a</sup>
1-10	44 (33.3)	14 (25)	30 (39.5)	
11-20	48 (36.4)	20 (35.7)	28 (36.8)	
> 20	40 (30.3)	22 (39.3)	18 (23.7)	
Lifelong psychosis (yes)	79 (59.8)	32 (57.1)	47 (61.8)	0.586 <sup>b</sup>
Lifelong psychotic episodes <sup>d</sup>				0.175 <sup>a</sup>
1-5	54 (48.2)	18 (40)	36 (53.7)	
6-10	33 (29.5)	15 (33.3)	18 (26.9)	
>10	25 (22.3)	12 (26.7)	13 (19,4)	/
Polarity predominantly negative (yes)	36 (27.7)	18 (32.1)	18 (24.3)	0.324 <sup>b</sup>
Rapid cycling (yes)	43 (34.4)	20 (39.2)	23 (31.1)	0.347 <sup>b</sup>
Suicide attempt (yes)	50 (37.9)	22 (39.3)	28 (36.8)	0.775 <sup>b</sup>
Lifelong dependence or substance abuse (yes)	19 (14.4)	5 (8.9)	14 (18.4)	0.125 <sup>b</sup>
Lifelong anxiety disorder	51 (38.9)	22 (40)	29 (38 2)	0.831 <sup>b</sup>
Personality disorder (yes)	57 (43.2)	25 (44.6)	32 (42.1)	0.771 <sup>b</sup>
Current mood stabilizer use (yes)	127 (96.9)	53 (94.6)	74 (98 7)	0.185 <sup>b</sup>
Current lithium use (yes)	94 (71.2)	36 (64.3)	58 (76.3)	0.131 <sup>b</sup>
Current antidepressants use (yes)	18 (13.8)	10 (17.9)	8 (10.8)	0.249 <sup>b</sup>
Current anti psychotics use (yes)	68 (52.3)	32 (58.2)	36 (48.0)	0.251 <sup>b</sup>
Current benzodiazepine use (yes)	39 (29.8)	21 (37.5)	18 (24)	0.095 <sup>b</sup>

ECT: Electroconvulsive therapy; BD-I: Bipolar Disorder type I; SD: sexual dysfunction Data are expressed by n (valid %).

<sup>a</sup> Mantel-Haenszel Chi-Square test for trend.

<sup>b</sup> Pearson Chi-Square test.

<sup>c</sup>Asthma, hypothyroidism, hyperthyroidism, diabetes, cardiovascular diseases, dyslipidemia or obesity.

<sup>d</sup> N=122.

The comparison between the groups of patients with and without SD, regarding sociodemographic variables, showed that the subgroup with SD was composed mostly of women (p=0.001), with a tendence of being older (p=0.030) and a lower proportion of paid occupancy (p=0.001). Regarding clinical variables, they tended to have more years of disease duration (p=0.033) and a higher

proportion with a long duration of untreated illness (to first treatment with a mood stabilizer) (DUI) above 5 years (p=0.010). No differences were observed between the two groups with regards to the medications used (Table 1). Patients with SD had worse QoL scores in all domains measured by WHOQoL-BREF, compared to those without SD (figure 1).

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Image 1 – Quality of Life for patients with BD-I with and without SD

BD-I: Bipolar Disorder type I; WHOQOL-BREF: World Health Organization's Quality of Life Instrument – Short Version; SD: sexual dysfunction

After adjusting for variables with p<0.1 in the univariate analysis and for those with clinical plausibility (N=125), only women (OR 7.09, 95% CI 2.12 – 23.72; p=0.001) and DUI with mood stabilizer > 5 years (OR 2.75, 95% CI 1.02 – 7.43; p=0.046) remained associated with SD. The presence of paid occupation (OR 0.29, 95% CI 0.10 – 0.82; p=0.019) and age between 30-49 years (compared with age  $\geq$  50 years) (OR 0.28, 95% CI 0.09 – 0.90; p=0.033) were less associated with SD (Table 2).

Table 2 – Multivariate analysis through binary logistic regression of factors associated with SD in patients with BD-I (N=125)

Variable	В	Adjusted OR	95% CI	р
18-29 years	-1.12	0.33	(0.60 – 1.77)	0.195
30-49 years	-1.27	0.28	(0.09-0.90)	0.033
$\geq$ 50 years <sup>a</sup>				
Female	1.96	7.09	(2.12-23.72)	0.001
Paid occupation	-1.22	0.29	(0.10-0.82)	0.019
Duration of illness	-0.06	0.94	(0.48-1.85)	0.860
Delay to first mood stabilizer treatment >5 years	1.01	2.75	(1.02-7.43)	0.046
Current lithium use	-0.28	0.76	(0.29-1.98)	0.571
Current antidepressant use	0.36	1.44	(0.39-5.24)	0.581
Current antipsychotic use	0.65	1.91	(0.78-4.68)	0.159
Current benzodiazepine use	0.77	2.15	(0.86-5.38)	0.100

CI: Confidence interval; OR: Odds Ratio.

<sup>a</sup> Reference category.

<sup>b</sup> Variable included as ordinal (whereas the difference between 1-10yrs and 11-20yrs is similar to 11-20yrs and >20yrs).

When comparing patients with BD-I and HC, it was observed that the group of patients had higher frequency of SD (p<0.001), more clinical comorbidities (p=0.001) and more personality disorder (p=0.002). This group also showed lower frequency of paid occupancy (p=0.001) (Table 3).

Table 3- Sociodemographic and clinical characteristics of patients with BD-I and controls

Variable			p <sup>a</sup>
	BD - I	Controls	$- \bigcirc$
	(n=132)	(n=61)	$\sim$
			$\bigcirc$
Age (years)			0.015
18-29	19 (14.4) <sup>b</sup>	19 (31.1) <sup>b</sup>	×
30-49	75 (56.8) <sup>b</sup>	24 (39.3) <sup>b</sup>	
$\geq 50$	38 (28.8)	18 (29.5)	
Female gender (yes)	98 (74.2)	44 (72.1)	0.757
with partner (yes)	51 (38.6)	27 (44.3)	0.459
Individual income (yes)	94 (71.8)	45 (75)	0.640
Religious affiliation (yes)	111 (84.1)	54 (88.5)	0.416
Paid occupation (yes)	41 (31.3)	35 (57.4)	0.001
Years of schooling <sup>c</sup>	Y		0.013
≤9	15 (12.1) <sup>b</sup>	13 (26.5) <sup>b</sup>	
10-12	47 (37.9)	22 (44.9)	
> 12	62 (50) <sup>b</sup>	14 (28.6) <sup>b</sup>	
Lifelong smoking (yes)	42 (31.8)	12 (21.1)	0.133
Physical activity (yes)	39 (29.5)	24 (40.7)	0.131
Clinical comorbidity (yes)	84 (63.3)	23 (37.7)	0.001
Personality disorder (yes)	57 (43.2)	12 (20)	0.002
Sexual dysfunction (yes)	56 (42.4)	10 (16.4)	< 0.001

Data are expressed by n (valid %).

<sup>a</sup> Pearson Chi-Square test.

<sup>b</sup> Statistically different groups after post-hoc analysis through adjusted standardized residuals.

<sup>c</sup> N= 173.

<sup>d</sup> Asthma, hypothyroidism, hyperthyroidism, diabetes, cardiovascular diseases, dyslipidemia or obesity.

All phases of sexual response were significantly more altered in patients when compared to controls. There was a higher prevalence of changes in orgasm in both groups (Table 4).

Table 4 – Sexual function in patients with BD-I and HC

Variable				
variable	BD - I HC			
	(n=132)	(n=61)		
	Ŝ			
Modified sexual attraction <sup>b</sup>	47 (35.6)	11 (18)	0.013	
Excitation/lubrication or erection	57 (43.2)	15 (24.6)	0.013	
modified	69 (52.3)	18 (29.5)	0.003	

Modified orgasm<sup>d</sup>

BD-I: bipolar disorder type I; HC: healthy controls

Data represented by n (valid %).

<sup>a</sup> Pearson Chi-Square test.

<sup>b</sup> Score  $\geq$  4 on Arizona Sexual Experiences Scale first item.

<sup>c</sup> Score  $\geq$  4 on Arizona Sexual Experiences Scale second and/or third item.

<sup>d</sup> Score  $\geq$  4 on Arizona Sexual Experiences Scale fourth and/or fifth item.

After adjusting for sociodemographic and clinical variables with p<0.1 in the univariate analysis, BD-I group was more associated with SD than HC (OR 3.67, 95% CI 1.55 – 8.67; p=0.003) (Table 5).

Variable	β	Adjusted OR	95% CI	р
BD-I (reference: healthy controls)				0.003
Age (years)	1.30	3.67	(1.55-8.67)	
18-29	-0.76	0.47	(0.16-1.35)	0.160
30-49	-1.19	0.30	(0.13-0.70)	0.005
$\geq 50^{a}$		1		
Female gender (yes)	1.66	5.26	(2.08-13.27)	< 0.001
Paid occupation (yes)	-0.85	0.43	(0.20-0.90)	0.025
Clinical comorbidity (yes)	0.08	1.09	(0.52-2.27)	0.823

Table 5 – Multivariate analysis using binary logistic regression of factors associated with SD in the overall sample: patients with BD-I and HC.

SD: sexual dysfunction; BD-I: bipolar disorder type I; HC: healthy controls; IC: Confidence interval; OR: Odds Ratio. <sup>a</sup> Reference category.

#### Discussion

Although sexual function is an important component when assessing the QoL of a population, this topic is still scarce in medical literature, especially when it comes to BD- patients.

In our study using the ASEX, the prevalence of SD in BD-I patients was 42.4%, and the difficulty in achieving orgasm was the most affected domain in both groups (patients and HC). This rate described in the patient's group differs from those found in other cross-sectional studies, probably because some methodological differences, such as included or not symptomatic patients, control of the type of medication and the type of scales applied. One of these studies analyzed 114 patients with BD in euthymic state, using only mood stabilizers, and showed an average SD higher (50%) than ours. But, in line with our results, it found that the SD is more frequent in women and older age individuals <sup>32</sup>. Another study, which evaluated only male patients with BD in symptomatic remission and in use of antipsychotics, showed SD in 66% of the sample at least in one phase of the sexual response cycle<sup>33</sup>. In this study, the most common SD was erectile

dysfunction (47.1%), followed by decreased desire/libido (39%), ejaculatory dysfunction (17.6%) and difficulty with orgasm (14.8%). The higher prevalence of SD, when compared to our study, may be explained by the sample being composed only of men and with higher frequency use of antipsychotics, considering that this class of medication can alter dopaminergic transmission and increase prolactin levels, which has already been associated with changes in the sexual response cycle <sup>34</sup>

Another research, which also evaluated 100 patients with BD in remission who were using only lithium, found a lower SD rate than ours (37%)<sup>24</sup>. In addition, in this study, the most reported altered domains were arousal and libido, not orgasm as we described. Such divergence might be related to the fact that there is only lithium in the entire study sample, which is a drug already more associated with decreased libido<sup>35</sup>. In this line, other mood stabilizers, such as valproate, can also lead to hormonal changes that interfere in the sexual response cycle <sup>23</sup>. In fact, regarding sexual function, the use of psychotropics, including antipsychotics, is described as one of the factors that is mostly associated to SD, with impact in all phases of the sexual cycle<sup>11,34</sup>, as just described in patients with schizophrenia <sup>36</sup>.

Despite the knowledge of the interferences of psychotropics in the sexual function, we did not find a significant difference between the medications used in patients with and without SD, probably because almost all patients demonstrate homogeneity in the use classes of medication. In this sense, it is also important to highlight that few patients were using ADs (37%), that are closely associated with SD, and a small part of the sample was on monotherapy, which makes difficult to analyze the association between groups of medications individually.

Our study found an association between the female gender and the presence of SD in the group of patients, which is in line with the current literature, as demonstrated by the review of García-Blanco et al (2020)<sup>32</sup>. Another important aspect found in our study was the association between DUI with mood stabilizer and the presence of SD. However, until the present moment, we did not find, in the literature, a similar result. This is highly relevant, once it demonstrates that intrinsic factors of BD could be associated with development of SD, which may be reasonable, since brain circuits involved in the pathophysiology of BD, such as the hypothalamic-pituitary-adrenal axis, the amygdala and monoaminergic

circuits, are also involved in the sexual response<sup>3738</sup>. Besides that, the untreated disease leads to worse outcomes throughout life, such as a greater tendency to suicidal behavior, a greater number of hospitalizations, a higher frequency of depression, mania/hypomania episodes<sup>39</sup>. Furthermore, these findings reinforce the need for an early diagnosis and initiation of adequate treatment in patients with BD.

#### Quality of life and sexual function in patients' group

In the QoL assessment, all domains are more impaired in patients with SD compared to those without dysfunction. This result is in agreement with a study carried out including only women with BD, which demonstrated that a higher level of suffering with sexual function was related to worse QoL domains<sup>40</sup>. In fact, this finding is in line with studies that demonstrate that patients with mood disorders have worse QoL compared to the general population, as confirmed a recent meta-analysis <sup>41</sup>. In this context, the understanding of SD as one of the associated factors becomes essential, as it may be more present in patients with BD and major depression <sup>42</sup>.

#### Sexual function in BD-I patients compared to health controls

Our results show that BD-I patients had a higher prevalence of SD when compared with HC. Also, all domains of sexual function measured by ASEX were more impaired in patients than in HC, which can be seen in some previously published studies.

In line with our results, a recent cross-sectional study, which evaluated 80 patients with BD-I and BD-II in remission compared with 70 HC, found that BD patients had significantly poorer sexual functioning globally and were twice more likely to feel unsatisfied with their sexual life than the control group. These findings were associated with some markers of disease severity, such as hospitalization, suicide attempt and longer duration of illness, for example<sup>43</sup>.

A cross-sectional study that evaluated the sexual function of 60 patients with BD-I compared to 60 HCs reported worse sexual function scores in patients than in controls, despite the lack of a definition of euthymia and the use of measurement scales different from ASEX, such as the International Index of Erectile Function (IIEF) for men and the Female Sexual Function Index (FSFI) for women <sup>44</sup>. Another study that compared the sexual function and suicidal behavior of HC and patients with mood disorders (BD and unipolar depression) demonstrated higher rates of SD in patients, with an impact on all phases of sexual function. Despite the fact that the patients were evaluated without euthymia control, which may interfere in the study results, their findings were similar to our study. In this study, changes in sexual function in the patient's group were associated with greater chances of suicidal behavior <sup>45</sup>.

On the other hand, one study performed only with women found no significant difference in the prevalence of SD in patients with BD (24.6%) compared to controls (16.8%). This result could be explained because of the use of different scales to assess sexual function between the groups and the absence of euthymia criteria. However, this study, in line with ours, reports that women with BD were significantly more often sexually distressed than the control population, with also a negative impact on their QoL<sup>40</sup>.

#### Limitation and strengths

This study has some limitations: the cross-sectional design does not allow for causal inferences; it was not possible to control the use of other clinical medications (eg, antihypertensive drugs) or comorbidities, which are known to influence sexual function, we did not investigate pain during sexual function. On the other hand, there are strengths: as far as we know, this study is a pioneer in the use of a specific scale, the ASEX, to measure sexual function in patients with BD-I who were evaluated only in a state of symptomatic remission, with strict euthymia criteria. Beyond that, we also measured the QoL of these patients and evaluated its association with sexual function, which is rarely found in the literature. In addition, we compared a sample of patients with HC, which has a great impact on the understanding of factors that may be associated with SD in different individuals.

#### Conclusions

This study found a high prevalence of SD in BD-I patients compared to HCs. The patients showed impairment in all phases of sexual response, which may be related to the possible severity of this phenomenon in this population. The presence of SD in patients was more associated with female gender, older age, and with a longer DUI to adequate BD treatment. Patients with SD also had more impairment in all QoL domains, compared to those without SD. Despite knowing that human sexual response is largely influenced by several factors, these findings reinforce the importance of a regular assessment of sexual function in clinical practice, and an early diagnosis and medical interventions in patients with BD. Moreover, it is necessary more detailed investigation on sexual function and its repercussions in the course of the disease of this population.

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#### **Conflict of interest declaration**

The authors report no conflicts of interest.

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