Journal of Affective Disorders 243 (2019) 103–107

Contents lists available at ScienceDirect

Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad

Research paper

Clinical features of differential diagnosis between unipolar and bipolar depression in a drug-free sample of young adults

André Machado Patella[a], Karen Jansen[b], Taiane de Azevedo Cardoso[b,c,*], Luciano Dias de Mattos Souza[b], Ricardo Azevedo da Silva[b], Fábio Monteiro da Cunha Coelho[d]

[a] Catholic University of Pelotas, RS, Brazil
[b] Graduate Program in Health and Behavior, Translational Science on Brain Disorders, Catholic University of Pelotas, RS, Brazil
[c] Department of Psychiatry and Behavioural Neurosciences, McMaster University, Hamilton, ON, Canada
[d] Federal University of Pelotas, RS, Brazil

ARTICLE INFO

Keywords:
Bipolar disorder
Bipolar depression
Major depressive disorder
Unipolar depression
Differential diagnosis
Mood disorders

ABSTRACT

Introduction: Subjects with bipolar disorder suffering of a depressive episode are frequently misdiagnosed as unipolar depression, being important studies assessing the differential diagnosis between bipolar and unipolar depression.
Objective: To assess the sociodemographic and clinical features of drug-free young adults in a depressive episode of bipolar or unipolar disorder in order to identify factors that may differentiate these psychiatric conditions.
Methods: This is a cross-sectional study with 241 young adults aged between 18 and 29 years who were evaluated using the Structured Clinical Interview for DSM-IV (SCID). The sample comprised patients with BD (n = 89) and major depressive disorder (n = 152), experiencing a depressive episode and not using psychoactive drugs or illicit psychoactive substances.
Results: The characteristics associated with bipolar depression were being male ($p < 0.001$), with a family history of BD ($p = 0.013$), a higher frequency of childhood traumatic experiences ($p = 0.001$), younger age of onset of mood disorder ($p = 0.004$), many previous depressive episodes ($p = 0.027$), greater severity of depressive symptoms ($p < 0.001$) and day/night reversal ($p = 0.013$). Those with unipolar depression showed a higher frequency of biological rhythm disturbances ($p < 0.001$), and diurnal preference ($p = 0.028$).
Limitations: The sample has not included subjects with severe suicide risk, a possible important marker in differentiate unipolar from bipolar depression.
Conclusion: Some clinical aspects may contribute to an early differential diagnosis of both bipolar and unipolar depression even in the initial stages of the disease.

1. Introduction

Bipolar Disorder (BD) is one of the most disabling diseases in the world (Angst et al., 2011; WHO, 2008). Almost half of all patients with BD type I and approximately three- quarters of those with BD type II will first have an episode of depression (Goodwin and Jamis, 2010; Tondo et al., 2014). The diagnostic criteria for bipolar disorder (BD) are based on the presence of a manic or hypomanic episode to distinguish from unipolar depression (Perlis et al., 2006). A delay in diagnosis of BD, or even errors in diagnosis can cause a delay in treatment, and therefore, prolong suffering (Bowden, 2005).

Misdiagnosis of BD as unipolar depression is a serious clinical problem (Goodwin and Jamis, 2010). Multiple studies indicate that the symptoms of BD can be detected if observed carefully, in approximately one-quarter of the patients diagnosed with major depressive disorder (MDD). Other studies suggest that the prevalence of bipolar characteristics in patients with MDD is close to 50% (Angst et al., 2011). Some possible causes for the difficulty in determining a correct diagnosis include the lack of perception of the patient to the manic symptoms as opposed to symptoms of depression, the idea of hypomania as "good/normal times", the omission of a family member in the diagnostic evaluation, focus on euphoric mood rather than irritability and dysphoria (hypomania), and finally, the intention of making a diagnosis for which there are several effective treatments (unipolar depression)

* Corresponding author at: Department of Psychiatry and Behavioural Neurosciences, McMaster University 100 West 5th Street, Suite G110, Hamilton, ON L8N 3K7, Canada.
E-mail address: taianeacardoso@hotmail.com (T.d.A. Cardoso).

https://doi.org/10.1016/j.jad.2018.09.007
Received 13 April 2018; Received in revised form 29 July 2018; Accepted 9 September 2018
Available online 11 September 2018
0165-0327/

(Goodwin and Jamis, 2010). In addition, it is important highlight that in the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) (APA, 2013) added the "mixed features" as a specifier for depressive disorders. Thus, a patient who presents a depressive episode with three or more (hypo)manic symptoms is diagnosed as a mixed depressive disorder. This criterion turns closer and more difficult to differentiate the diagnosis of major depressive disorder from bipolar disorder.

Several factors have been proposed as potential predictors of BD diagnosis based only on the differences between the early clinical presentations of bipolar and unipolar depressed patients. Currently, however, no criteria have been clearly established for psychiatric clinical practice. Some predictive factors include: (a) family history of bipolar disorder, (b) onset of the disease before the age of 25 years, (c) multiple (more than 4) depressive episodes, and (d) substance abuse (Tondo et al., 2014). However, there are very few population-based studies with a drug-free sample of young adults in the early stages of the disease.

The present study aimed to investigate the potential clinical differences between unipolar and bipolar depression in a drug-free sample of young adults, in order to identify factors that may differentiate both psychiatric conditions.

2. Methods

This is a cross-sectional study conducted at the Clinic of Research and Extension in Mental Health of the *Universidade Católica de Pelotas* (UCPel). It is part of a major study approved by the Research Ethics Committee of the institution (protocol number 2010/24). Participants were evaluated by three well-trained psychologists at the Hospital Universitário São Francisco de Paula (HUSFP) located at Pelotas, Brazil. BD and MDD were diagnosed based on the Structured Clinical Interview for DSM (SCID). Young adults diagnosed with MDD and those with bipolar disorder (BD) that were in a depressive episode participated in the present study. The exclusion criteria were to be enrolled in a current psychological or psychiatric treatment, use of any psychopharmacologic medication, severe suicide risk (those with current plans) and use of any psychoactive substance (except tobacco and alcohol).

The sociodemographic data were obtained through an interview (sex, age and education). The Hamilton Depression Rating Scale (HAM-D) was used to assess the depressive symptoms. This instrument contains 17 items that are used to rate the severity of depression. A score of 0–7 is considered to be normal. Scores of 20 or higher indicate moderate, severe, or very severe depression (Hamilton, 1967). The reliability of the scale between the evaluators has been consistent in several studies (Moreno and Moreno, 1998). To distinguish bipolar from unipolar depression among young patients, the absence or the presence of symptoms, regardless of the intensity, was considered.

Biological rhythm disruption was measured with the Biological Rhythms Interview of Assessment in Neuropsychiatry (BRIAN). The BRIAN consists of 18 items measuring sleep, activity, social and eating pattern. All items are evaluated on a four-point scale, where 1 = not at all, 2 = rarely, 3 = sometimes, and 4 = often; higher scores denote greater disturbance in the corresponding biological rhythm. Giglio et al. developed and validated the BRIAN scale for the Brazilian population (Giglio et al., 2009). The items scored "no difficulty" and "rarely difficulty" were grouped into "absence of difficulty"; while the items "sometimes" and "often" into "presence of difficulty".

Abuse/dependence on tobacco and alcohol was assessed through the Alcohol, Smoking and Substance Involvement Screening Test (ASSIST) (Henrique et al., 2004). This instrument consists of eight questions about the use of tobacco, alcohol, cannabis, cocaine, amphetamine type stimulants, inhalants, sedatives, hallucinogens, opiates and 'other drugs'. The substance abuse/dependency variable was calculated from the sum of the scores for each substance class. A score of 0–3 is considered to be indicative of occasional use, 4–15 as indicative of abuse and greater than or equal to 16 as suggestive of dependence. This instrument has been validated and adapted for the Brazilian population. In the present study, abuse and dependence constituted the only category in the statistical analysis.

The frequency of childhood trauma was evaluated using the Childhood Trauma Questionnaire (CTQ). The CTQ is a 28-item, self-report measure widely used to assess history of childhood abuse and neglect in individuals up to the age of 18 years. This scale measures five categories of childhood maltreatment: Emotional, Sexual and Physical Abuse (EA, SA and PA), and Emotional and Physical Neglect (EN and PN). It uses a 5-item Likert scale. Currently, the CTQ is widely used in clinical, forensics or research (Grassi-Oliveira et al., 2014). In this study, the items were added in order to analyze the differences in frequency of childhood traumatic experiences between bipolar and unipolar depressed young people.

Data processing was performed using double-entry in Epi-Info 6.04d and then submitted to statistical analysis using SPSS 22 for Windows. Descriptive data were expressed as the mean (μ) and standard deviation (±) or absolute (n) and relative (%) frequency. The bivariate analysis was conducted using the chi-square test and the t test. The multivariate analysis was conduct using Poisson regression to adjust the analysis for potential confounders. We considered potential confounders the variables with p-values < 0.20 in the crude analysis. Poisson regression was also used to obtain estimates of prevalence ratios (PR). Statistically significant associations were considered when $p < 0.05$.

3. Results

A total of 241 young adults, who were not taking any psychotropics, were included in the present study. Of these, 152 young adults were unipolar and 89 bipolar. Further, 78.9% of these subjects were female with unipolar depression and 50.6% were bipolar females ($p < 0.001$). The variables 'age' and 'education' showed no significant differences between the groups (Table 1).

Regarding the clinical characteristics, the BD subjects showed a higher frequency of family history of BD ($p = 0.013$), higher scores for childhood traumatic experiences ($p = 0.001$), early age of onset of mood disorder ($p = 0.004$), and higher proportion of previous depressive episodes ($p = 0.027$), as compared to subjects with unipolar depression. Disturbances in biological rhythm were higher in subjects with unipolar depression ($p < 0.001$), while the severity of depressive symptoms was higher among subjects with bipolar depression ($p < 0.001$) (Table 1).

Table 1
Demographic and clinical characteristics of participants.

Demographic and clinical characteristics	Unipolar depression n (%) / μ (±)	Bipolar depression n (%) / μ (±)	*p*-value
Sex			<0.001
Female	120 (78.9%)	45 (50.6%)	
Male	32 (21.1%)	44 (49.4%)	
Age (in years)	23.07 (± 3.01)	23.06 (± 3.37)	0.969
Education (in years)	10.83 (± 3.53)	10.21 (± 3.66)	0.222
Family history of BD	4 (2.6%)	9 (10.1%)	0.013
Frequency of childhood trauma	46.33 (± 14.26)	53.47 (± 15.04)	0.001
Age of illness onset	17.86 (± 4.60)	16.18 (± 4.06)	0.004
>three depressive episodes	58 (38.2%)	47 (52.8%)	0.027
Alcohol abuse	44 (28.9%)	30 (33.7%)	0.439
Tobacco abuse	50 (32.9%)	36 (40.4%)	0.237
Depression symptoms (HDRS)	13.52 (± 5.04)	16.32 (± 6.79)	<0.001
Biological rhythm (BRIAN)	51.12 (± 13.97)	44.62 (± 10.06)	<0.001
Sleep/social	20.55 (± 4.80)	17.72 (± 6.09)	<0.001
Activity	9.97 (± 3.12)	8.00 (± 3.58)	<0.001
Eating pattern	9.43 (± 3.03)	8.27 (± 3.48)	0.010