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Accuracy of the number of previous episodes reported by patients with bipolar disorder

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Abstract

Background: The number of previous episodes in patients with BD is a variable widely used for both clinical and research purposes. The aim of this study was to compare the number of episodes retrospectively reported by euthymic BD subjects with that registered by their psychiatrists during a follow-up period.
Methods: Fifty euthymic patients with BD and more than 2 years of follow-up were retrospectively asked in a standardized fashion about the number of hypomanic/manic and depressive episodes suffered during that period. Patient-reported outcomes were compared with the number of episodes registered by psychiatrists in a life chart during the same period.
Results: The mean follow-up of patients was 66.70 months. There was a mean difference of 2.74 episodes between reports of patients' and psychiatrists' reports during the complete follow-up period; Intraclass correlation coefficient was 0.40 (CI95% = 0.15–0.61). This difference increased with the duration of the follow-up period ($R = 0.33$, $p = 0.023$) and with the number of episodes occurred during that ($R = 0.32$, $p = 0.023$). The difference between patient-reported and clinician-rated in the number of depressive during the follow-up period was more pronounced in BDII than in BDI ($Z = -2.47$, $p = 0.014$), and it correlated with the number of previous depressive episodes at baseline ($R = 0.28$, $p = 0.047$) and subclinical depressive symptoms ($R = 0.41$, $p = 0.003$).
Conclusions: The number of previous episodes referred by patients with BD is not an accurate measure of the true number of episodes suffered. The theoretical and practical implications of these findings are discussed.

1. Introduction

Bipolar disorder (BD) is a recurrent illness characterized by mood episodes of hypomania/mania and depression alternating with periods of euthymia. Studies conducted in the pre-pharmacological era as well as recent studies of BD patients taking prophylactic medication consistently showed a high tendency to recurrences in most cases [1]. Likewise, longitudinal studies reported that both patients with bipolar I and II disorder spent around 50% of the time with affective symptoms, with a considerable amount of time suffering subclinical symptoms in addition to threshold symptoms of hypomania/mania and depression [2,3].

The number of previous episodes in patients with BD is a variable of great relevance for both clinical and research purposes. As psychiatrists/psychologists we use the number of previous episodes in daily practice to determine the predominant polarity in an individual patient, the risk of further recurrences, the response to treatments used in the past, and to select the current medication regimen among others [4–6]. On the other hand, as researchers we use the number of previous episodes as an indicator of clinical severity in studies of BD about clinical course of the disorder, physiopathology, or neuropsychology among others [7–9]. However, despite its widespread use, the number of previous episodes would be difficult to pinpoint. First, the picture of a high rate of recurrence in a disorder with a symptomatic structure fluctuating along the full range

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of severity and polarity within the same patient over time highlights the difficulty to collect the precise number of previous episodes. In addition to this issue inherent to the clinical course of BD, there is another problem related to difficulties in recalling the past, especially for those patients with cognitive impairments [10,11]. Therefore, the accuracy patient-reported number of previous episodes should be clarified. Likewise, some large studies use the number of previous hospitalizations as a proxy of the number of previous episodes regarding the clinical course/severity of patients with BD [12,13]. Although the number of previous hospitalizations might be easier to ascertain, to the best of our knowledge no studies have specifically evaluated the relationship between this variable and the longitudinal course of BD in terms of number of episodes.

Then, the aim of this study was to compare the number of episodes referred retrospectively by patients with euthymic BD along a follow-up period with those registered by their psychiatrists during the same period. A second aim was to assess the relationship between the number of previous hospitalizations and the number of mood episodes experienced by patients during the follow-up period. We hypothesized that there could be a significant difference in the number of episodes reported by patients and psychiatrists.

2. Methods

Fifty subjects were consecutively selected from the outpatients population of the Bipolar Disorder Program of the Favaloro University with the following inclusion criteria: age between 18 and 60 years old; diagnosis of BD type I (BDI) or BD type II (BDII) according to DSM-IV using the Structured Clinical Interview for DSM-IV (SCID) [14]; euthymic (defined by Hamilton Depression Rating Scale ≤9 and Young Mania Rating Scale ≤8) for at least 8 weeks; and a follow-up period of more than 24 uninterrupted months. Exclusion criteria were: antecedent history of substance abuse, history of mental retardation, neurological disease, or any unstable clinical condition (like hypothyroidism) that could affect recall ability. The study was approved by the hospital ethics committee and all subjects gave written informed consent for their participation after receiving a complete description of the study.

2.1. Clinical assessment

In addition to the SCID, all subjects were evaluated with the Hamilton Depression Rating Scale (HDRS) [15] and Young Mania Rating Scale (YMRS) [16]. Additional demographical (age, gender, years of education) and clinical information at baseline (before the onset of the follow-up period: age at illness onset, length of illness, bipolar subtype, previous manic/hypomanic and depressive episodes, and number of hospitalizations) was obtained from clinical charts and direct patient interviews. When possible, attempts were made to verify these historical data with third-party reports (medical records, family interview, etc.).

2.2. Follow-up assessment

In our program, patient's course of illness is documented at each visit (with intervals usually around 1–2 months) with a modified life charting technique rated by his/her psychiatrist on a weekly basis (Fig. 1). This life chart technique was used in previous studies by our group [17,18] and was developed without the knowledge or purpose of the present work. Patients with more than 24 uninterrupted months of follow-up were retrospectively asked in a standardized fashion about the number of hypomanic/manic and depressive episodes suffered during that period. The obtained outcomes were compared with the number of episodes registered by psychiatrists in the life chart during the same period. For the purposes of this study we considered two types of episodes from life chart: 1) depressive episode: a period of two or more weeks with mild, moderate, or severe depression; 2) hypomanic/manic episode: a period of at least one week with mild, moderate, or severe mania. Comparisons were made between patients and psychiatrists (life chart) with regard to the number of episodes reported during both the whole follow-up and the last year of this period.

Patients were treated by their psychiatrists under naturalistic conditions over the follow-up period, and the necessary psychotropic medications in accordance to published guidelines were prescribed.

2.3. Data analysis

The assumption of normality and homoscedasticity of each variable was analyzed with the Kolmogorov–Smirnov normality test and Levene test respectively. Since most of variables regarding number of episodes both reported from patients and psychiatrists during the follow-up period were skewed, non-parametric tests were used. Differences between the number of episodes reported by patients and psychiatrists (life chart) were analyzed as two related samples using the Wilcoxon signed rank test. Differences in the number of episodes registered during the follow-up period for independent subgroups of patients (e.g. clinical subtype or with and without psychotherapy/psychoeducation) were analyzed with the Mann–Whitney test. Association between continuous variables was assessed with the Spearman's correlation coefficient. Despite the asymmetric distribution of certain variables, results are also expressed as mean and standard deviation to improve understanding.

3. Results

Clinical characteristics of the sample at baseline of follow-up period are summarized in Table 1. The mean follow-up was 66.70 months (standard deviation, SD = 27.11; median = 66, range = 24–120). During this period psychiatrists registered in

	January	Etc.	
+4			Severe Mania (YMRS≥26)
+3			Moderate Mania (YMRS≥16 and <25)
+2			Mild Mania (YMRS≥9 and <15)
+1			Subclinical Mania (YMRS>4 and <8)
0			Euthymic (YMRS<4 and HDRS<4)
-1			Subclinical Depression (HDRS>5 and <9)
-2			Mild Depression (HDRS≥10 and <15)
-3			Moderate Depression (HDRS≥16 and <25)
-4			Severe Depression (HDRS≥26)

YMRS: Young Mania Rating Scale; HDRS: Hamilton Depression Rating Scale.

Fig. 1. Criteria for assigning mood state scores in life charts.

the life chart a mean of 4.70 (SD = 3.01; median = 4, range = 0–12) mood episodes, with 1.56 (SD = 1.79; median = 1, range = 0–7) hypo/manic episodes, and 3.14 (SD = 2.53; median = 3, range = 0–11) depressive episodes.

Only 18% of the patients reported the same outcome as their psychiatrist during the complete follow-up, while 62% under-reported affective episodes and 20% over-reported these events. Differences in the number of episodes reported by patients and their psychiatrists during the total follow-up period and in the last year of follow-up are showed in Table 2. Taking into account the skewed nature of these variables, two procedures were employed to assess the concordance between episodes registered by patients and psychiatrists along the follow-up period. First, we calculated the Kendall's coefficient of concordance for total (W = 0.21, df = 1, p = 0.001), hypomanic/manic (W = 0.13, df = 1, p = 0.011), and depressive (W = 0.21, df = 1, p = 0.001) episodes. In addition, intraclass correlation coefficient was calculated for total episodes registered by patients and psychiatrists during the whole follow-up after performing a logarithmic transformation to achieve a normal distribution and homoscedasticity of the variables (ICC = 0.40, CI95% = 0.15–0.61, df = 49, p = 0.001).

We later explored variables that could be associated with differences in the number of episodes reported by patients and their psychiatrists during the follow-up period. As we expected, the higher number of episodes that occurred during follow-up was associated with a greater difference between the number reported by patients and psychiatrists for total (R = 0.32, p = 0.023), hypomanic/manic (R = 0.37, p = 0.009), and depressive (R = 0.34, p = 0.014) episodes (Fig. 2). Likewise, the difference in the total number of episodes between patients' and psychiatrists' reports increased with duration of follow-up period (R = 0.33, p = 0.023). This difference was similar between patients with BDI and BDII (Z = -0.35, p = 0.72), and with and without individual psychotherapy (Z = −1.15, p = 0.25) or psychoeducational program (Z = −0.35, p = 0.73). In addition, there was no correlation between the difference in the total number of episodes reported by patients and psychiatrists during follow-up with clinical and demographic variables at baseline (Table 1) (all p > 0.05). Similarly, there was no association between the difference in the number of hypomanic/manic episodes reported by patients and psychiatrists during the follow-up with the same demographic and clinical variables (all p > 0.05). Finally, the difference in the number of depressive episodes reported by patients and psychiatrists during the follow-up period was more pronounced in BDII (mean = 2.41, SD = 1.74; median = 2, range = 0–7) than in BDI (mean = 1.70, SD = 3.88; median = 1, range = 0–20) (Z = −2.47, p = 0.014), and it also correlated with the number of previous depressive episodes at baseline (R = 0.28, p = 0.047) and HDRS (R = 0.41, p = 0.003). There was no association between the difference in the number of depressive episodes reported by patients and psychiatrists during the follow-up with the remaining demographic and clinical variables explored (all p > 0.05).

Lastly, we explored the relationship between traditional variables of clinical course referred by patients at baseline (number of previous hypomanic/manic and depressive episodes, and number of previous hospitalizations) with number of episodes registered by their psychiatrist during the follow-up period. The number of previous hypomanic/manic episodes at baseline correlated with the number of hypomanic/manic episodes during follow-up (R = 0.40, p = 0.004), but no with the number of total (R = −0.012, p = 0.93) or depressive episodes (R = −0.25, p = 0.088). The number of previous depressive episodes at baseline correlated with the number of depressive (R = 0.36, p = 0.012) and hypomanic/manic episodes (R = −0.33, p = 0.021) during follow-up, but not with the total number of episodes (R = 0.076, p = 0.60).

Table 1
Clinical characteristics of patient sample at baseline of follow-up period (values are expressed as mean, standard deviation is shown in brackets).

Age (years)	47.27 (12.71)
Education (years)	14.80 (3.07)
Age at onset	28.47 (12.67)
Clinical subtype (n, % type I)	27 (54)
No. of previous hypo/manic episodes	3.31 (3.84)
No. of previous depressive episodes	4.16 (4.69)
YMRS score	0.18 (0.63)
HDRS score	1.96 (2.42)
Mood stabilizers (n, %)	50 (100)
Antipsychotics (n, %)	28 (56)
Antidepressants (n, %)	14 (38)
Benzodiazepines (n, %)	13 (36)
Individual psychotherapy (n, %)	14 (38)
Group psychoeducation (n, %)	9 (18)

There was no association between the number of previous hospitalizations with the number of total (R = −0.13, p = 0.37), hypomanic/manic (R = 0.20, p = 0.18), and depressive (R = −0.27, p = 0.058) episodes registered during the follow-up period. There was also no correlation between the number of previous hospitalizations with the number of total (R = −0.047, p = 0.82), hypomanic/manic (R = 0.082, p = 0.70), and depressive (R = −0.033, p = 0.87) episodes registered during the follow-up period when only patients with BDI were selected. We repeated these last analyses considering the intensity (mild, moderate, and severe) of hypomanic/manic and depressive episodes registered during the follow-up period; the number of previous hospitalizations only correlated with severe hypomanic/manic episodes (R = 0.38, p = 0.008).

Table 2
Differences in the number of episodes reported by patients and their psychiatrists during the total follow-up period and in the last year of follow-up.

	Differences mean (SD); median (range)	Wilcoxon signed rank test
Total follow up		
Total episodes	2.74 (3.5); 2 (0–20)	(Z = −3.54, p < 0.001)
Hypomanic/manic episodes	1.20 (2.11); 1 (0–12)	(Z = −1.91, p = 0.057)
Depressive episode	2,00 (3.07); 2 (0–20)	(Z = −3.46, p = 0.001)
Last year of follow-up		
Total episodes	0.38 (0.63); 0 (0–3)	(Z = −0.39, p = 0.69)
Hypomanic/manic episodes	0.14 (0.35); 0 (0–1)	(Z = −0.38, p = 0.70)
Depressive episode	0.26 (0.53); 0 (0–2)	(Z = −0.64, p = 0.52)

4. Discussion

With the aim to explore the accuracy of the number of previous episodes reported by BD subjects, we retrospectively asked patients about the number of episodes experienced during a follow-up period and compared their reports with the number of episodes registered in a life chart by their psychiatrists during that period. One of the main findings of the study was that psychiatrists registered a mean of 4.70 episodes during a follow-up of around 5 years, while patients reported a mean difference of 2.74 episodes in this period. This difference was significant for the number of total and depressive episodes, and could be explained mainly by under-reporting of episodes in about two thirds of the patients. It is possible to speculate that the lesser amount of episodes of hypomania/mania in comparison with depression occurring in patients with BD in our study and in previous longitudinal studies [2,3] could contribute to the smaller difference observed between patients and psychiatrists in hypomanic/manic episodes. In contrast, there was no difference between patients and their psychiatrists in the number of hypomanic/manic or depressive episodes reported in the last year of follow-up. This result, together with the positive correlation observed between the difference in the number of reported events and the years of follow-up, suggests that the number of previous episodes referred by patients may be more accurate for recent periods and more inexact for distant time points. There was a low-to-moderate level of concordance between patient-reported and psychiatrist-registered number of episodes during the follow-up period, which suggests that the number of previous episodes reported by patients may be a relatively inaccurate proxy for the true number of episodes.

The difference between patients' and psychiatrists' reports increased with the number of episodes occurred in the follow-up period, suggesting that self-reported history of previous episodes might be less accurate in patients with multiple episodes. This could be particularly true for patients with a high number of previous depressive episodes. We also found that patients with BDII may be less accurate in the record of previous episodes, which is probably linked to the higher rate of depressive recurrences associated with this subtype of disorder [19,20]. In addition, subclinical depressive symptoms were associated with a poorer register of the number of depressive episodes suffered during follow-up, which could be linked to the effect of these symptoms on recall ability [21,22].

On the other hand, the number of hospitalizations might not be a marker of clinical course in terms of number of episodes, and it could only be a proxy for the number of severe manic episodes. In contrast, patients with more previous episodes at baseline had higher number of episodes during the follow-up period, suggesting that patients with worse clinical course tended to be the same before and during the follow-up period. Interestingly, more depressive episodes at baseline were associated with more depressive episodes during follow-up, and the same for hypomanic/manic episodes, suggesting also the stability of the predominant polarity over time as it was found in previous studies [23].

These findings may have clinical and theoretical implications if they were confirmed in future studies. From a clinical point of view, accuracy could reach its lowest levels with increasing duration of the disorder and successive recurrences (e.g. in elderly patients with an early age at onset). Likewise, patients with BDII and prevalent subclinical depressive symptoms (e.g. BDII patients comorbid with borderline personality traits) may also be a group of patients prone to inaccurate register of previous depressive episodes. Beyond the individual and group psychoeducational approach to improve the recognition and register of mood episodes, patients may be encouraged to keep a written record of successive episodes. This information could be very useful when the patient is examined by a new psychiatrist or psychologist (i.e. when he/she change of treatment or is hospitalized). Some additional issues should be considered when the number of previous episodes is used for research purposes. First, if the risk of underreporting is higher in distant time points and lower in recent years,

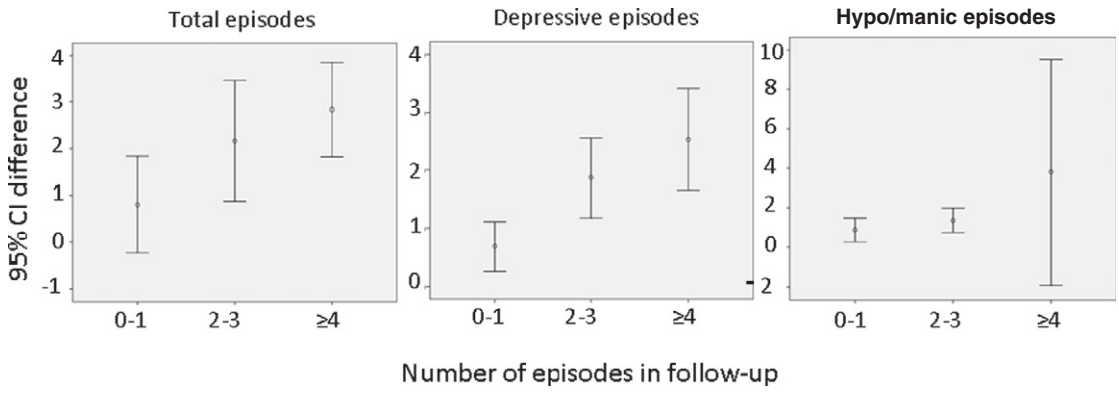

Fig. 2. Differences between patients' and psychiatrists' reports by number of episodes occurred during follow-up.

studies about the clinical course of BD obtaining the number of episodes retrospectively might find a biased result suggesting increased cycling throughout the evolution of the disorder. Second, if the risk of underreporting increases with the number of previous episodes, correlational studies may underestimate the true degree of association with several clinical or pathophysiological characteristics. For example, this could be the case of neurocognitive studies that found an association between the number of previous episodes and deficits in verbal memory, attention, and executive functions (for a review, see Robinson and Ferrier [7]). The same could happen with pathophysiological studies that have linked the number of previous episodes with the level of biomarkers or volumetric changes in the brain [24,25]. Finally, the number of previous hospitalizations must not be taken as a marker of the number of previous episodes as it usually is in studies on the clinical course of BD. Instead, previous hospitalizations may be considered as a proxy for severe manic episodes.

Several limitations must be taken into account. First, although the follow-up period was quite extensive, the sample size was relatively small. This particular might have blurred the differences between subgroups of patients in the accuracy of the registration of episodes (i.e. with and without psychoeducational program). Second, both criteria of hypomanic/manic and depressive episodes employed in this study were not those defined in the DSM-IV. However, a change from euthymia to a period longer than a week with a YMRS higher than 9 points, or a period longer than 2 weeks with an HDRS score higher than 10 points, resembles quite a hypo/manic or depressive episode respectively. In addition, we considered only patients with uninterrupted period of follow-up, then excluding patients with more chaotic evolutions which presumably could have a worse record of the number of previous episodes. Likewise, ours is a tertiary care center and, therefore, it is possible that patients have a worse clinical course (and registration of episodes) than patients with BD in the general population. Taken together, these results should be considered preliminary and be subject to further replication.

5. Conclusions

The number of previous episodes referred by patients with BD is an inaccurate measure of the true number of episodes suffered. Despite the preliminary nature of the results, the findings of this study would be useful when considering the number of previous episodes for both clinical and research purposes. Furthermore, our findings reinforce the advantages of prospective studies when evaluating the clinical course and severity of patients with BD.

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