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Research paper

Residual depressive symptoms, sleep disturbance and perceived cognitive impairment as determinants of functioning in patients with bipolar disorder

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ABSTRACT

Background: Many patients with bipolar disorder (BD) experience residual symptoms during their inter-episodic periods. The study aimed to analyse the relationship between residual depressive symptoms, sleep disturbances and self-reported cognitive impairment as determinants of psychosocial functioning in a large sample of euthymic BD patients.

Methods: This was a cross-sectional study of 468 euthymic BD outpatients. We evaluated the residual depressive symptoms with the Bipolar Depression Rating Scale, the sleep disturbances with the Pittsburgh Sleep Quality Index, the perceived cognitive performance using visual analogic scales and functioning with the Functioning Assessment Short Test. Structural equation modelling (SEM) was used to describe the relationships among the residual depressive symptoms, sleep disturbances, perceived cognitive performance and functioning.

Results: SEM showed good fit with normed chi square=2.46, comparative fit index=0.94, root mean square error of approximation=0.05 and standardized root mean square residuals=0.06. This model revealed that residual depressive symptoms (path coefficient =0.37) and perceived cognitive performance (path coefficient=0.27) were the most important features significantly related to psychosocial functioning. Sleep disturbances were indirectly associated with functioning via residual depressive symptoms and perceived cognitive performance (path coefficient=0.23).

Conclusions: This study contributes to a better understanding of the determinants of psychosocial functioning during the inter-episodic periods of BD patients. These findings should facilitate decision-making in therapeutics to improve the functional outcomes of BD during this period.

1. Introduction

Bipolar disorder (BD) is a severe and highly recurrent mental illness affecting more than one per cent of the world's population (Grande et al., 2016; Merikangas et al., 2011). A substantial proportion of BD patients (30–60%) are living with significant functional impairment even after reaching clinical remission (MacQueen et al., 2001). According to the World Health Organisation, BD is among the leading causes of years lost due to disability (WHO, 2008).

The inter-episode period (also named euthymia) was regarded as an asymptomatic phase in which BD patients were in clinical remission. However, this classical perspective has been challenged since a large

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number of euthymic patients experience residual symptoms during periods of apparent clinical stability (Soreca et al., 2009). New evidence suggests that BD is not only a recurrent mental illness but also a chronic disease associated with the persistence of residual symptoms shaping an individual presentation. Several studies have shown the persistence of depressive symptoms (Judd et al., 2003), cognitive impairments (Bourne et al., 2013; Mann-Wrobel et al., 2011), sleep and circadian rhythm disturbances (Geoffroy et al., 2014; Mondin et al., 2016; Sylvia et al., 2012) and emotional dysregulation (Strejilevich et al., 2013) in euthymic BD patients. Interestingly, residual symptoms appear to impact the natural course of BD and represent potential predictors of long-term outcome. Residual depressive symptoms are associated with an increased risk of recurrence (de Dios et al., 2012; Judd et al., 2008) and, together with persistent cognitive deficits and sleep disturbances, are important predictors of functional impairment (Altshuler et al., 2006; Bas et al., 2015; Baune and Malhi, 2015; Bonnín et al., 2010; Dittmann et al., 2008; Gitlin and Miklowitz, 2016; Harvey et al., 2005; Marangell et al., 2009; Pinho et al., 2015; Rosa et al., 2010; Wingo et al., 2009, 2010).

Moreover, an interaction between those residual symptoms may exist—e.g. residual depressive symptoms seem to worsen cognitive deficits, producing a subsequent negative impact on functioning (Bonnín et al., 2014), or poor sleep and cognitive functioning seem to be associated with poor work performance (Boland et al., 2015). However, the exact nature of the interdependent relationships among residual depressive symptoms, cognitive impairment, sleep disturbances and functioning, and the relative contribution of each of these residual symptoms, remains unclear.

The observational OPTHYMUM study aimed to examine residual symptoms in BD patients who were recruited in the euthymic period. Previous analyses showed that residual symptoms (mainly residual depressive symptoms, perceived cognitive impairment and sleep disturbances) have an impact on functioning (Samalin et al., 2014, 2016a) and their severity seems to be negatively related to the duration of the euthymia (Samalin et al., 2016b). However, these previous reports did not examine the direction and the structure of the relationships between residual symptoms and functioning. It would be of interest to contribute to a better understanding of the negative impact of these residual symptoms on the functioning of BD patients and it could have implications for its improvement.

Based on previous research (Boland and Alloy, 2013; Bonnín et al., 2012, 2014; Bowie et al., 2010; Giglio et al., 2010; Gruber et al., 2009; Leboyer and Kupfer, 2010; Rosa et al., 2013; Russo et al., 2015; Volkert et al., 2015), our hypotheses were that: i) residual depressive symptoms and perceived cognitive performance primarily have a direct effect on functioning; ii) sleep disturbances have an indirect effect on functioning via perceived cognitive performance and residual depressive symptoms; iii) residual depressive symptoms might have a moderate indirect effect on functioning via perceived cognitive performance; and iv) sleep disturbances might have a moderate direct effect on functioning.

The aim of the present study was to examine a comprehensive model based on structural equation modelling (SEM) that integrates the interrelationships between residual depressive symptoms, sleep disturbances and self-reported cognitive impairment as determinants of psychosocial functioning in a sample of euthymic BD patients in real-life conditions.

2. Material and methods

2.1. Study participants

This study is based on a sample of 468 adult outpatients with BD from a multi-centre, cross-sectional, non-interventional study conducted in France between April and October 2012 (Samalin et al., 2014).

An enlarged directory of psychiatrists randomly assigned from a previous French study on bipolar disorder was used (Nuss et al., 2012) to recruit a large number of patients. A total of 139 French psychiatrists in hospital and office-based settings agreed to participate to the study.

The inclusion criteria were as follows: (1) age over 18 years; (2) diagnosis of BD type I or type II according to DSM-IV-TR criteria; and (3) in euthymic period for at least six months after the last acute mood episode. Euthymia was defined according to the symptomatic remission criteria for a mood episode established by the International Society for Bipolar Disorder (ISBD) Task Force (Tohen et al., 2009), as a Young Mania Rating Scale (YMRS; Young et al., 1978) total score < 8 and a Bipolar Depression Rating Scale (BDRS; Berk et al., 2007) total score ≤ 8.

The exclusion criteria were (1) inability to understand or complete the self-administered questionnaires and (2) participation in a clinical trial.

The procedures followed in the study were approved by an independent national ethics committee (CPP Sud-Méditerranée IV). Written informed consent was obtained for included subjects after the nature of the procedures was explained.

2.2. Data collection

The following data were collected by trained psychiatrists through a patient interview and complemented by clinical records.

1. Socio-demographic information: age, gender, marital status, educational status and employment status.
2. Clinical characteristics: BD type; age at onset of BD; age at first prescription of mood stabilizer; predominant polarity of BD (at least two-thirds of past major depressive episodes defined a depressive predominant polarity; at least two-thirds of past hypomania/mania defined a manic predominant polarity; other cases defined a not specified predominant polarity (Colom et al., 2006)); presence of rapid cycling; number of hospitalizations. Pharmacological treatment was also recorded.
3. Residual symptoms: residual depressive symptoms were measured using the BDRS (Berk et al., 2007). It is a semi-structured, observer-rated scale for clinical assessment of bipolar depression. It consists of 20 items (including one item concerning sleep disturbance and one item concerning memory and concentration) that are rated from 0 to 3 on a Likert-type scale. The BDRS total score ranges from 0 to 60, such that higher scores reflect more severe depressive symptoms. Sleep quality and sleep disturbance were assessed using the Pittsburgh Sleep Quality Index (PSQI) (Buysse et al., 1989). The PSQI is a self-reported questionnaire that assesses seven dimensions of sleep over a one-month period: subjective quality, latency, duration, efficiency, disturbances, use of sleep medication and daytime dysfunction. It consists of 19 self-rated items and the total score ranges between 0 and 21, with higher scores indicating worse sleep quality. Residual cognitive symptoms (cognitive performance) perceived by the patients over the previous month (memory dysfunction, concentration impairment, psychomotor retardation and impairment of planning ability) were self-assessed using four nine-point visual analogic scales (VAS) (Samalin et al., 2014). The VAS evaluates the degree of impairment of each variable. Subjects indicate for each item their level of impairment with a trait between two extreme conditions: a score of 1 indicates no impairment, while a score of 9 indicates the worst impairment. The total score of the cognitive VAS ranges between 4 and 36.
4. Functioning: the French version of the Functioning Assessment Short Test (FAST) was used to assess disability in BD patients (Claire et al., 2012; Rosa et al., 2007). The FAST is a valid and reliable instrument assessing functioning in BD patients. It provides an objective evaluation of functioning in six specific areas: autonomy, occupational functioning, cognitive functioning, financial issues,