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Research report

Family history of a mood disorder indicates a more severe bipolar disorder

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ABSTRACT

Background: In the clinical setting, patients with bipolar disorder (BD) are often asked about potential family history (FH) of mood disorders. The aim of the present study was to examine differences between BD patients with FH of a mood disorder, and those without, on clinical, personality and social functioning characteristics, as well as on the symptomatic course of the disorder.
Methods: Data was collected from the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD). For this report, we included 2600 patients, 1963 of those reported having a first-degree family member with a mood disorder, and 637 reported of no such FH. We investigated the impact of FH on socio-demographic, clinical, personality and quality of life variables, as well as on symptomatology during the first year of treatment.
Results: Patients reporting FH of a mood disorder had an earlier age at onset of depression/mania, more phases, rapid cycling and more suicide attempts. Across different assessments, patients with FH showed consistently elevated depressive symptoms, such as lower concentration and energy, higher suicidal ideation, as well as increased racing thoughts and distractibility within the manic spectrum of symptoms. Further, the FH group had lower quality of life, higher neuroticism and higher personality disorder scores compared to patients without FH.
Limitations: Information on FH was obtained through the proband.
Conclusions: Overall, BD patients reporting FH of a mood disorder showed a worse clinical profile upon presentation for treatment and a more symptomatic course of the disorder.

1. Introduction

Approximately 1–4% of the population suffers from Bipolar Disorder (BD) (Hirschfeld et al., 2003). Patients with BD are likely to suffer from psychological and biological changes that can lead to a poor quality of life and engagement in dangerous or risky behaviors. BD runs in families; family, twin, and adoption studies suggest heritability rates of 63–79% (Smoller and Finn, 2003). Furthermore, the type of bipolar disorder has been suggested to be heritable – that is, Bipolar I is more common in relatives of probands with the same type, and vice versa for Bipolar II (Benazzi, 2007).

Understanding the type of risk that family history may pass on serves two main purposes. Firstly, by identifying the factors that cluster in BD families, researchers may be able to better characterize heritable sub-phonotypes of the disorder and therefore more likely to uncover its underlying genetic architecture. Secondly, although clinicians acknowledge the importance of assessing family history in bipolar patients, little is known about how this familial risk is clinically manifested in the symptomatology and quality of life of the patient (Martinez and Fristad, 2013). This information could be of clinical, even prognostic, use.

Few studies have investigated correlates of family history in BD patients. Early research has suggested an earlier age of onset of the disorder in BD patients with familial history (Mendlewicz et al., 1972). Further, family history of mania was associated with more affective episodes in 251 patients with BD, more hospitalizations, but no earlier age of onset (Winokur et al., 1986). In a group of Bipolar I patients with a family history of mood disorders, an earlier age at onset (<20 years), a higher frequency of episodes and a higher chance of hospitalization was observed compared to patients without familial history (Mrad et al., 2007). In line with the observations of an early age of onset indicating familial loading, pediatric BD is observed 15 times more among patients with family history of BD (Pavuluri et al., 2006). Furthermore, in patients with early-onset depression a family history of BD was found to predict future bipolar disorder (Thase, 2006), and affected siblings have a similar age of onset of the disorder (O'Mahony et al., 2002).

Other clinical characteristics that have been associated with family history of a mood disorder include rapid cycling (Lish et al., 1993; Saunders et al., 2008), however, evidence of no familial

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relationship has also been shown (Bauer et al., 1994; Coryell et al., 1992; Fisfalen et al., 2005). More frequent episodes have also been reported in patients with family history (Fisfalen et al., 2005; Nolen et al., 2004), although such history was not associated with symptom severity, during one year, in 258 BD patients (Nolen et al., 2004). BD patients with family history of mood disorders were also more likely to have comorbid axis I disorders, such as panic disorder, psychosis, substance abuse/dependence, and suicidal thoughts (Saunders et al., 2008), but another study found no evidence of association between family history and risk of axis I comorbidity in BD patients (McElroy et al., 2001). In addition, psychotic features have been associated with a family history of a mood disorder (O'Mahony et al., 2002; Souery et al., 2012). In addition to clinical characteristics, a positive family history of mood disorders has been associated with impaired neurophysiological functioning as measured in neuroimaging studies (Drevets et al., 2002). In parallel, behavioral assessments in offspring of BD patients have shown impairments in sustained attention tasks (Diwadkar et al., 2011).

Family and clinical studies suggest that a family history of mood disorders may influence the clinical course of BD and comorbidity with other disorders, but results are often inconsistent. Most studies to date suffer from small sample sizes and cross-sectional designs. The aim of the present report was to examine the effect of familial loading on clinical, personality and social functioning characteristics, in a large cohort of bipolar patients from the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) study. More specifically, we hypothesized that the presence of at least one first-degree family member with a mood disorder (mania and/or depression) will be associated with the following patient characteristics: (a) a worse clinical profile at baseline in terms of disorder characteristics, psychiatric comorbidity and suicide risk (b) a more symptomatic course of the disorder.

2. Methods

2.1. Participants

STEP-BD was a prospective study, aiming to develop and expand knowledge on the management and treatment of BD and evaluate the longitudinal outcome of patients with this disorder. Patients gave both oral and written consent for participation, in line with the Declaration of Helsinki. Exclusion criteria of the study were few: unwillingness to follow the assessments or not being able to do so, refuse to give consent or be below 15 years of age. Patients were followed by trained psychiatrists and treated according to the evidenced-based current therapy guidelines (Sachs et al., 2003). Overall, 4360 patients were included in the STEP-BD; data from the Standard Care Pathway (SCP) were used for this report ($n=4107$). Patients in the SCP could belong to any spectrum of bipolar disorder and received pharmacological interventions as clinically indicated by the principles of evidence-based treatment and published guidelines, updated annually in the STEP-BD Clinicians Handbook. The protocol promoted the application of evidence-based treatments at regular clinical sessions during treatment, according to the needs of the patient and did not follow compliance to a specific treatment algorithm. This naturalistic study used ongoing assessments of treatment and outcome information.

2.2. Measures

Family history (FH) was assessed using the self-report Family History form (part of the STEP-BD patient-packet forms) (Sachs et al., 2003) at baseline. The form asked patients to report whether any biological first-degree family member (mother, father, brother, sister, son, and daughter) suffered from mania and/or depression (which may or may not have been formally diagnosed). Patients were also asked to report "unknown" if they did not know their FH, or "none" if none of their relatives had serious difficulties with a disorder.

Several measures were utilized to investigate patients' clinical status. The diagnosis of bipolar disorder, and psychiatric Axis I comorbidities (according to DSM-IV) have been assessed with the Mini International Neuropsychiatric Interview (MINI Version 4.4) (Sheehan et al., 1998). The Affective Disorder Evaluation (ADE) form (Sachs, 2004), was an intake assessment form used by practicing clinicians and designed to document various aspects on history nd current state of illness, medical history and mental status. It included a modified version of the mood and psychoses modules from the Structured Clinical Interview for DSM-IV, which was assessed upon study entry together with a socio-demographic form (Sachs, 2004). The ADE form was also used to assess history of suicide attempt. According to the ADE, a psychiatric diagnosis was categorized as none, probable or definite, whereas using the MINI a current or lifetime diagnosis (present or absent). For determining psychiatric comorbidity in this report both the ADE and MINI data were taken into account in order to minimize missing values.

The Clinical Monitoring Form (CMF) is a standardized scale that was used to assess the clinical progress of every patient at each visit (Sachs et al., 2002). It was administered by CMF-certified study clinicians and it assessed specific manic and depressive symptoms at each follow-up visit. Recordings were made on 9 depressive symptoms and 7 manic symptoms, which ranged from +2 (much more), to − 2 (much less), and 0 indicated no change (Sachs, 2004). Data from 94 clinicians who had obtained training and certification on the CMF showed intraclass correlations for degree of agreement on depressive and manic symptoms with ratings ranging from 0.828 to 0.997 (Schneck et al., 2008). The number of CMFs completed for each patient was recorded since treatment was naturalistic and patient visits occurred according to clinical demand.

The Young Mania Rating Scale (YMRS) (Young et al., 1978) and Montgomery-Åsberg Depression Rating Scale (MADRS) (Montgomery et al., 1985) were administered to patients upon study entry, and every three months thereafter, in order to determine illness severity. For both the MADRS and the YMRS – the mean number of each symptom and mean total number of symptoms during the first year (visits: baseline, 3-, 6-, 9-, 12-month) were computed. The number of visits for each patient was also recorded.

The 60-items Neuroticism Extroversion Openness Five Factor Inventory (NEO-FFI) was used to evaluate the personality traits defined in five basic dimensions (Costa et al., 1992; McCrae and John, 1992). Hopelessness was measured using Beck's Hopelessness Scale, a 20-item true/false questionnaire assessing patient's feelings of hope toward different aspects of life, such as future, work and accomplishment (Beck et al., 1974). The Personality Diagnostic Questionnaire (PDQ) was used to assess personality disorders according to DSM-IV; it consists of a set of 99 true/false statements and the total score reflects a general index of personality disorder (Fossati et al., 1998). The Quality of Life Enjoyment and Satisfaction short Form (QLES-SF) evaluated the amount of satisfaction felt by the patients in the past week prior administration; higher scores indicate greater satisfaction (Endicott et al., 1993). The mean score over the first year (visits: baseline, 3-, 6-, 9-, 12-month) was computed.

2.3. Statistical analysis

SPSS 20.0 was used for the statistical analyses. As primary analysis, we examined differences between patients with and without a first-degree relative with mania and/or depression. For