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Research report

Childhood abuse, family history and stressors in older patients with bipolar disorder in relation to age at onset

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ABSTRACT

Objectives: The aim of this study is to explore the family history of psychiatric disorders, childhood abuse, and stressors in older patients with Bipolar Disorder (BD) and the association of these variables with the age at onset of BD.
Methods: The Questionnaire for Bipolar Disorder (QBP) and the Mini International Neuropsychiatric Interview (MINI-Plus) were obtained from 78 patients aged 60 and over to determine diagnosis, age at onset of the first affective episode, childhood abuse, family history of psychiatric disorders and past and recent stressful life events.
Results: Increased family history of psychiatric disorders was the only factor associated with an earlier age at onset of BD. Less family history of psychiatric disorders and more negative stressors were significantly associated with a later age at onset of the first (hypo)manic episode.
Limitations: Age at onset, history of childhood abuse, and past stressful life events were assessed retrospectively. Family members of BD patients were not interviewed.
Conclusions: Our findings suggest that age at onset can define distinct BD phenotypes. More specifically there was a stronger heredity of BD and other psychiatric disorders in patients with an early age of onset of BD. Negative stressors may play a specific role in patients with a late age at onset of a first (hypo)manic episode.

1. Introduction

Studies have suggested a multifactorial etiology for Bipolar Disorder (BD), including both biological and psychosocial factors, with genetic and environmental factors interacting (Brietzke et al., 2009; Caspi and Moffitt, 2006; Gama et al., 2013). Identification of the pathophysiological determinants of BD is a major challenge with implications for the early detection, prevention, and treatment strategies of this disorder (Etain et al., 2008). Subtyping bipolar patients by age at onset may help identify different phenotypes that require specific treatment strategies, since an early onset (EO) has a less favorable course (Geoffroy et al., 2013). For example, a study showed that early onset of BD in general was associated with a more severe historical disease course, as reflected in greater comorbidity for most Axis I disorders, greater chronicity represented by more mood episodes and a greater proportion of days depressed, and greater lifetime risk of suicide attempts (Perlis et al., 2004). Also functioning and quality of life at study entry was significantly poorer among early- and very-early-onset subjects (Perlis et al., 2004). The cut off for defining early onset bipolar disorder (EOBD) and late onset bipolar disorder (LOBD) ranges across studies from 30 to 65 years, but is most often set at age 50 (Depp and Jeste, 2004). However, this cut off at age 50 is debated upon as it is in the middle of the later peak of life time incidence rates of BD (Kroon et al., 2013).

Some of the pathophysiological determinants for BD may be more associated with EOBD than LOBD. Studies found that a family history of affective disorder, psychotic disorder or substance abuse is more common in EOBD than in LOBD (Leboyer et al., 2005; Post et al., 2013b). Moreover, a family history of affective disorder is associated with a more severe course of BD, including an earlier onset, more episodes, more suicide attempts and lower quality of life (Antypa and Serretti, 2014; Berutti et al., 2014). In addition to hereditary factors, severe childhood abuse is also associated with an earlier onset of BD (Etain et al., 2008; Garno et al., 2005; Suppes et al., 2001). In younger adults with BD it was found that the

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prevalence of any type of abuse ranges from 36% (Leverich et al., 2001) to 49.9% (Hyun et al., 2000). In studies reporting different types of abuse, verbal abuse is more frequent (50.3–52.0%), compared to physical (23.0–33.8%), or sexual abuse (27.0–34.1%) either during childhood or adolescence (Leverich et al., 2001; Post et al., 2013a; Suppes et al., 2001). Causal relationships between BD and psychosocial stressors are complex to assess, as it is often difficult to establish whether a stressor was the cause or consequence of the illness (Alloy et al., 2005; Hosang et al., 2012; Johnson, 2005). Still stressors contribute to the onset of bipolar disorder as well as to subsequent episodes (Tsuchiya et al., 2003; Urosevic et al., 2008). A recent study found that the numbers of stressful life events in childhood (including abuse) and in the year prior to the last episode of BD were significantly higher in more severe BD patients with an earlier onset (Post et al., 2013a).

The observation of an earlier age at onset in patients with a positive family history of severe affective disorders can be explained by a higher genetic risk, but alternatively, the emotional distress of having an affected parent or other close family member could also trigger an earlier onset of symptoms. The burden of a positive family history may be enhanced by exposure to more stressors and possible childhood abuse early in life. Post et al. (2013a) found an association between an early age at onset and physical or sexual abuse in childhood in BD patients with a parental load for affective disorder. Alternatively, severe affective symptoms during childhood may predispose to disrupted interactions with parents, increasing the risk for emotional or even physical abuse.

The present study aims to explore associations between age at onset of BD and a family history of psychiatric disorders, childhood abuse, and past stressors in bipolar patients aged 60 and over. We hypothesize that patients with an EOBD have significantly more psychiatric disorders among first and second degree family members and have experienced more childhood abuse than patients with a later onset. Further, it is hypothesized that patients with LOBD have experienced significantly more negative or positive stressors prior to their first episode of BD, given the association of late-life mania with somatic or environmental causes (Shulman, 1997; Van Gerpen et al., 1999). To the best of our knowledge this is the first study exploring both hereditary and environmental aspects of late life BD with respect to the onset of BD.

2. Methods

2.1. Subjects

In this cross-sectional study all patients (both in- and outpatients) aged 60 and over with a diagnosis of BD who were treated in our institute during the year 2012 were recruited by a search of the computerized record keeping system of the Mental Health Organization (GGZ inGeest, Amsterdam, The Netherlands) and were considered eligible for inclusion (for details see (Dols et al., 2014)). Patients were included in the study only if the diagnosis of Bipolar I Disorder (DSM-IV-TR: 296.00-.06, 296.40-.46, 296.50-.56, 296.60-.66, 296.7), Bipolar II Disorder (DSM-IV-TR: 296.89), or Bipolar Disorder NOS (Not Otherwise Specified, DSM-IV-TR: 296.80) was confirmed with the Mini International Neuropsychiatric Interview Plus (MINI-Plus) (van Vliet and de Beurs, 2007). The MINI-Plus interview is common clinical practice during the diagnostic phase of patient care and the results of this interview are documented in a computerized record keeping system. Patients were excluded if they were unable to provide written informed consent (requested by their psychiatrist or community psychiatric nurse) due to inability to communicate in Dutch or English, mental retardation (IQ below 70, estimated on the basis of the patients' medical record), dementia (Mini Mental State Examination [MMSE] below 18 obtained during the interview) or because they were in a very unstable psychiatric condition (e.g. compulsory admission). Of all 139 eligible patients, 25 patients were excluded because of a language barrier ($n=1$), mental retardation ($n=4$), dementia ($n=8$), very unstable psychiatric condition ($n=1$), death ($n=1$), a different diagnosis ($n=10$: mood disorder NOS [$n=3$], personality disorder [$n=2$], schizoaffective disorder [$n=3$], cyclothymic disorder [$n=1$], recurrent depression [$n=1$]). Thirty-six patients were not willing to provide written informed consent for interviews, but of these patients 23 provided consent for medical record review (including a MINI-Plus interview). Seventy-eight patients were interviewed by the principal investigator or one of three trained psychology students. The study was approved by the Medical Ethics Committee (METC) of the VU University Medical Center, Amsterdam, the Netherlands.

2.2. Assessments

Demographic data (including age, sex, marital status, nation of birth, level of education, and living situation) were derived from the patients' medical records and confirmed during interview. The Global Assessment of Functioning score (GAF-score) is a measure by which the psychological, social and occupational functioning of a person is indicated by a score between 0 and 100 (American Psychiatric Association, 2003). GAF scores were separated for symptoms (GAF-s) and functioning (GAF-p). The 'Center for Epidemiologic Studies Depression Scale' (CES-D), a depression self-report questionnaire, was used to examine if participants experienced a depressive episode at the moment of the interviews (Radloff, 1977). Age at onset of BD, defined as the onset of the first affective episode, either (hypo)manic or depressive, and the age at first (hypo)manic episode were obtained from the MINI-Plus. The Dutch version of the Questionnaire for Bipolar Disorder (QBP) is an adaptation of the Enrollment Questionnaire as previously used in the Stanley Foundation Bipolar Network (Leverich et al., 2001; Suppes et al., 2001). The QBP-NL was used by the interviewer to investigate a family history of six mental disorders (depression, bipolar disorder, alcoholism, suicide or serious suicide-attempt, drug abuse, and psychosis) in first degree relatives (parents, siblings and offspring) and second degree relatives (grandparents) of the participants. The response options were: 1 (no), 2 (possible), 3 (probably), 4 (certainly: diagnosed or treated), or 5 (inapplicable). A specific psychiatric disorder was scored as 'disorder present in the family' if 'possible', 'probably' or 'certainly' was answered and as 'disorder not present in the family' if 'no' or 'unknown' was answered. Family history was quantified as the number of different types of mental disorders present in the whole family (not per family member), ranging between the minimum of 0 and maximum of 6.

The following aspects of childhood abuse were investigated: verbal or emotional abuse, physical abuse or ill treatment and assault or sexual abuse. In the QBP the following 3 questions were formulated: "Have you ever been verbally or emotionally abused (such as intimidation, threats, humiliation or serious insult which caused you some serious emotional damage) as a child?", "Have you ever been physically attacked or abused (i.e., are there experiences with physical injury or damage caused by another by beating, punches, kicking, biting, burning out, strangling or an attack with a weapon) as a child?" and "Have you ever been raped or sexually abused (i.e., are there experiences with sexual violence, sexual assault or forced sexual activity) as a child?". The data obtained by the QBP about abuse occurring in adolescence or adulthood were not used in this study. The response options were 0 (never), 1 (rarely), 2 (occasionally) or 3 (frequently). A childhood