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Research report

Temperament and prodromal symptoms prior to first manic/hypomanic episodes: Results from a pilot study

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ABSTRACT

Background: Prodromal symptoms prior to first episode mania/hypomania have been reported. However, the relationship between temperament and manic/hypomanic prodromal symptoms has not been investigated. We hypothesized that subjects scoring higher on cyclothymic and irritable temperament scales show more manic/hypomanic prodromal symptoms.

Method: Euthymic patients diagnosed with bipolar-I or -II disorder within 8 years underwent retrospective assessments with the Temperament Evaluation of Memphis, Pisa, Paris and San Diego-autoquestionnaire (TEMPS-A) and the Bipolar Prodrome Symptom Scale-Retrospective (BPSS-R).

Results: Among 39 subjects (36.1 ± 9.9 years, females = 59%, bipolar-I = 62%) 100% and 92.3% reported subthreshold mania (mean = 7.4 ± 2.9) or subthreshold depressive symptoms (mean = 2.4 ± 1.5), and 87.2% and 43.6% reported general psychopathology (mean = 3.2 ± 2.0) or subthreshold psychotic symptoms (mean = 0.7 ± 1.0) prior to their first hypo-/manic episode. Subjects with higher cyclothymic and irritable temperament scores showed more subthreshold symptoms prior to the first manic/hypomanic episode, mainly subthreshold hypo-/manic symptoms (cyclothymic temperament $r = 0.430$; $p = 0.006$; irritable temperament $r = 0.330$; $p = 0.040$), general psychopathology symptoms (cyclothymic temperament $r = 0.316$; $p = 0.05$; irritable temperament $r = 0.349$; $p = 0.029$) and subthreshold psychotic symptoms (cyclothymic temperament $r = 0.413$; $p = 0.009$). In regression analyses, cyclothymic temperament explained 16.1% and 12.5% of the variance of the BPSS-R total score ($p = 0.045$) and psychosis subscore ($p = 0.029$).

Limitations: Retrospective study, no control group, small sample size.

Conclusion: We present data, which indicate a relationship between cyclothymic and irritable temperament and prodromal symptoms prior to the first manic/hypomanic episode. These findings support the notion that assessing cyclothymic temperament to identify people at-risk of developing bipolar-I and -II disorder may help to increase the predictive validity of applied at-risk criteria.

1. Introduction

Intervening early in the course of bipolar disorder (BD), i.e., in the prodromal phase before the first full manic/hypomanic episode, may reduce the burden of BD, as this strategy has the potential to delay, lessen the severity of, or even prevent full-blown disorder (Berk, 2007; Conus et al., 2008; Correll et al., 2007b; McGorry et al., 2006; Salvadore et al., 2008).

Clinical features preceding the onset of BD can be identified (Bechdolf et al., 2012; Hauser and Correll, 2013; Hauser et al., 2007; Howes et al., 2011; Leopold et al., 2011; Skjelstad et al., 2010; Zeschel et al., 2013). Overall, the available retrospective and prospective studies reveal a pattern of putatively prodromal symptoms, of which mood liability/mood swings/cyclothymic features, depressed mood, racing thoughts, irritability, and physical agitation are the most commonly reported. As several different symptoms might be present prior to BD, a cluster of features, including distal and more enduring symptoms, such as personality

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traits, and more proximal, recently emerging or worsening clinical symptoms, including depressive and manic/hypomanic symptomatology, might best capture the bipolar prodrome. Recently, an at-risk syndrome or a Early Symptom Scale as prerequisites to develop targeted and early interventions in this population has been proposed and pilot evaluated (Bechdolf et al., 2010, 2012; Hauser et al., 2007). However, the predictive validity of such syndromes still needs to be improved. This could potentially be done by additional trait and state risk markers. In this context, the concept of temperament that has been explored in patients with syndromal BD (Aguiar Ferreira et al., 2013; Chiaroni et al., 2005; Gandotra et al., 2011; Henry et al., 2008; Mahon et al., 2013) as an endophenotypic trait of BD is of considerable interest for the characterization of the BD prodrome (Correll et al., 2007b; Kochman et al., 2005).

Temperament is defined as the baseline level of reactivity, mood and energy of a person that remains stable over time (Goldsmith et al., 1987; Nigg, 2006). Akiskal et al. (1995, 2005) postulated, that temperamental dysregulation is the fundamental pathology of mood disorders and proposed five different temperaments: depressive, cyclothymic, hyperthymic, irritable and anxious. The cyclothymic temperament presents with frequent and rapid shifts of mood and unstable energy and self-esteem. People with irritable temperament seem to be particularly critical, skeptical and complaining (Akiskal et al., 2005). Cyclothymic, hyperthymic and irritable temperament are more frequent in patients with BD than in patients with other psychiatric disorders or healthy controls (Dolenc, 2010; Hantouche et al., 1998; Mazzarini et al., 2009; Taylor et al., 2011). Further, in a small retrospective study Ozgurdal et al. (2009) reported that patients with BD who presented with cyclothymic and irritable temperament showed more mood swings prior to the onset of BD than patients without these temperament abnormalities. Cyclothymic temperament also predicted conversion to BD in children with depression using a liberal definition of manic symptoms lasting for more than 2 days (Kochman et al., 2005). Moreover people with genetic loading for BD present with higher scores on cyclothymic and irritable temperament than controls (Akiskal et al., 2005; Chiaroni et al., 2005; Evans et al., 2005; Mendlowicz et al., 2005).

However, to our knowledge, the relationship between temperament and the severity of prodromal symptoms of BD has not been examined. The aim of the present study was to explore retrospectively whether temperament correlates with prodromal symptoms prior to the first manic/hypomanic episode. We hypothesized that subjects who score higher on the cyclothymic and irritable temperament scale show more prodromal symptoms prior to their first manic/hypomanic episode.

2. Method

This was a retrospective uncontrolled study.

2.1. Subjects

Altogether, 44 participants with BDs according to the International Classification of Diseases (ICD-10), i.e., BD-I or -II, were recruited from three German University hospitals (Bochum, Dresden, Cologne) into a multi-center study. Five subjects were excluded: two subjects due to early discontinuation of the interview, and three because they did not complete the Temps-A Scale. At the time of the interview, all participants were outpatients in clinical remission who had experienced their first manic/hypomanic episode within 8 years. Interviews were conducted by a trained psychiatrist using the BPSS-R (Correll et al., 2007a), TEMPS-A (Akiskal et al., 2002), *Hamilton Depression Scale* [HAMD, 21] and the *Young Mania Rating Scale* [YMRS, 50]. Due to the retrospective nature of this study, all symptoms described in the results section below are self-reported by patients and related to their first prodromal phase of BD. Since we included patients with BD-II as well, we merged prodromal symptoms prior to a first hypomanic episode. Patients were aged between 18 and 65 and were fluent in reading and speaking German. The study was approved by the respective Ethical Committees and participants gave written informed consent.

2.2. Measures

Prodromal symptoms of BD were measured with the semi-structured *Bipolar Prodrome Symptom Scale-Retrospective* [BPSS-R, 14]. The BPSS-R systematically assesses 39 subthreshold symptoms prior to the first depressive, manic or hypomanic episode. Since we were interested in prodromal symptoms prior to the first manic/hypomanic episode, we only analyzed the data prior to the first manic/hypomanic episode and did not consider symptoms prior to the first depressive episode. The pre-onset symptoms were categorized into four subgroups: 1) subthreshold mania symptoms (i.e., lack of concentration, irritability, ideas of grandeur, overtalkativeness, racing thoughts, increased sexual interest, risky behavior, low sleep requirement, increased self-confidence and creativity), 2) depressive symptoms (i.e., lack of concentration, depressed mood, loss of vitality, loss of appetite/weight, sleep disorder, physical exhaustion, agitation, tiredness, feelings of worthlessness, suicidal thoughts and suicidal attempts), 3) general psychopathology symptoms (i.e., social isolation, loss of functioning, anxiety, compulsions, self-harming behavior, loss of patience, mood swings, creativity and provocative behavior), and 4) psychosis-spectrum symptoms (thought disorder, hallucination, suspiciousness and odd ideas). The BPSS-R total score consists of the addition of the four subscores, eliminating the duplicated items.

Temperament was assessed by the German version of the *Temperament Evaluation of Memphis, Pisa, Paris and San Diego-autoquestionnaire version* [TEMPS-A, 5]. This is a 110-item self-report, yes-or no-type questionnaire to quantify five different temperament types (depressive, cyclothymic, hyperthymic, irritable and anxious). The temperament was coded as clinically present if patients agreed to more than 70% of the items in accordance with Ozgurdal et al. (2009). The internal consistency (α) for the German version of the TEMPS-A varies from 0.75 to 0.84 (Akiskal et al., 2005). Test–retest-reliability ranges from 0.59 to 0.70 (Akiskal et al., 2005). Seven subjects filled out the short version of the TEMPS-A with 30 items. The internal consistency for the short version varied between 0.74 and 0.78 (Akiskal et al., 2005).

The current absence of major manic or depressive symptoms was confirmed by a HAMD of < 17 (Hamilton, 1960) and the YMRS of < 12 (Young et al., 1978).

2.3. Statistical analysis

Continuous data are presented with means (M), the standard deviation (SD), and categorical data with number of subjects and percentage. Temperament was analyzed with a dimensional score of the respective temperament-scale (percentage of agreement).

Differences between BD-I and -II subjects were calculated with χ^2- or t-tests.

The relationship between the five different TEMPS-A-scale scores and the four subscores of the BPSS-R was investigated through Pearson's correlation. To further analyze the data, a regression analysis with the inclusion of two temperament types was performed. The two temperament types, which correlated with the BPSS-R, were used as independent variables.