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Research report

Affective temperaments and neurocognitive functioning in bipolar disorder

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ABSTRACT

Background: There is evidence that patients with bipolar disorder (BD) score higher on affective temperament ratings compared to healthy controls (HCs). Moreover, unaffected relatives demonstrate similar patterns as BD patients suggesting that such temperaments are related to the genetic risk for BD and may serve as endophenotypes for the disorder. It is unknown whether affective temperaments are associated with other core features of BD, such as impairments in neurocognition. This study examined the relationship between affective temperaments and neurocognition in patients with BD and in HCs.
Methods: Temperaments were evaluated using the Temperament Evaluation of Memphis, Pisa, Paris, and San Diego, Auto-questionnaire version (TEMPS-A) in 64 patients with BD and 109 HCs. Neurocognitive functioning was evaluated using the MATRICS Consensus Cognitive Battery (MCCB). Correlational analyses between temperaments and cognition were conducted in BD and HC subjects.
Results: Data suggest that affective temperaments and neurocognition are correlated. In BD higher ratings of cyclothymia and irritability were associated with better processing speed, working memory, reasoning and problem-solving. In the HC group, increased irritability was related to worse performance on measures of attention and social cognition.
Limitations: Lack of functional outcome measures to evaluate the impact of temperaments and cognition on psychosocial functioning. It would be useful to test these findings on unaffected relatives of BD patients.
Conclusions: Cyclothymic and irritable temperaments are correlated with specific aspects of neurocognition in BD. This study is among the few exploring the dimensional relationship between temperaments and cognition in BD, and provides preliminary evidence for future studies investigating the neural and genetic mechanisms underlying the association between these variables.

1. Introduction

Bipolar disorder (BD) is a chronic psychiatric disorder characterized by an oscillation of depressive and (hypo)manic episodes, interspersed with periods of affective remission (DSM-V). Despite a general remission of overt affective symptoms during periods of euthymia, recent evidence suggests that illness features such as neurocognitive deficits persist beyond mood episodes and contribute to potentially persistent functional impairment (Arts et al., 2008; Bora et al., 2009; Robinson et al., 2006; Torres et al., 2007; Martínez-Arán et al., 2004). Cognitive deficits not only occur beyond the acute phase of the illness, but they are also present in unaffected relatives of patients with BD (Balanza-Martinez et al., 2008; Bora et al., 2009). This evidence supports the idea that neurocognitive deficits are potential endophenotypes for the disorder (Goldberg and Burdick, 2008; Gottesman and Gould, 2003; Glahn et al., 2004; Arts et al., 2008).

Identifying endophenotypes and investigating their relationship to other vulnerability factors are critical in gaining a better understanding of the complex architecture of BD. Within the framework of a dimensional conception of BD, in which core illness features are viewed as quantitative traits with a continuous distribution, it is important to understand how these dimensions may be interrelated.

In this study, we focused our attention on the relationship between neurocognitive functioning and affective temperaments. Temperamental factors are components of personality which are relatively stable over time (Goldsmith et al., 1987), specific to each individual, and reflect characteristics such as interpersonal style, energy level, and sensitivity and reactivity to internal and external stimuli. Since the

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beginning of the 20th century, Kraepelin (1921) recognized temperaments as steady personality characteristics out of which abnormal affective states may arise, potentially leading to the expression of a full-blown affective illness. Several researchers have developed this hypothesis into the concept of affective temperaments, that is, temperamental styles characterized by one or more of five main affective dimensions: anxious, irritable, cyclothymic, hyperthymic, and depressive (Akiskal, 1998; Akiskal and Mallya, 1987; Placidi et al., 1998). Conceptualized as quantitative dimensions, affective temperaments lie on a continuum from normality to pathology. In the last several decades, many studies have measured affective temperaments in different psychiatric samples, leading to the development of the Temperamental Evaluation of Memphis, Pisa, Paris, and San Diego-Autoquestionnaire (TEMPS-A) (Akiskal et al., 2005). Using this instrument, research suggests that patients with BD have higher ratings on several affective temperaments compared to non-clinical samples (Chiaroni et al., 2005; Evans et al., 2005; Mendlowicz et al., 2005) and that some temperaments might serve as markers of vulnerability for the disorder due to their over-representation in unaffected relatives of BD patients compared to healthy controls (Savits and Ramesar, 2006; Evans et al., 2005; Mendlowicz et al., 2005). A very recent study from our group showed that unaffected siblings of patients with BD present with affective temperament ratings that fall intermediate to affected BD probands and an unrelated healthy control sample (Mahon et al., 2013).

Taken together, this evidence suggests that affective temperament and neurocognitive functioning may represent dimensional endophenotypes in BD. Recent work suggests that, when affective temperament is measured categorically (i.e. when participants are determined to have a predominant affective temperament with subscale scores greater than or equal to one standard deviation above the mean), depressed patients with BD who had a predominantly hyperthymic temperament scored lower on measures of set-shifting and verbal working memory than depressed patients with BD with non-predominant affective temperaments (Xu et al., 2014). This work is the first to suggest that affective temperament may be associated with neurocognition in BD. However, no research has yet been conducted on the association between temperamental factors as a continuous, rather than a categorical measure, and neurocognitive functioning in BD. In the present work, we investigate the association between neurocognition and dimensionally-conceptualized affective temperaments during the euthymic phase. We first examined the levels of affective temperaments in patients with BD compared to a healthy control sample. We then explored potential relationships between affective temperaments and neurocognition in both the BD and healthy samples.

2. Methods

2.1. Participants

The sample was composed of a total of 173 participants: 64 patients with BD and 109 with HCs. Participants were recruited at two different sites: the Icahn School of Medicine at Mount Sinai and the Zucker Hillside Hospital (ZHH) – North Shore Long Island Jewish Health System.

BD sample: Inclusion criteria for patients included: 1) diagnosis of BD I or BD II or BD Not Otherwise Specified (NOS) ascertained using the Structured Clinical Interview for DSM-IV (SCID-IV) (First et al., 2002) and 2) current affective stability as measured by a score of <15 on the Hamilton Rating Scale for Depression (HRSD) (Hamilton, 1960) and by a score of <8 on the Clinician Administered Rating Scale for Mania (CARS-M) (Altman et al., 1994). *HC sample:* Healthy controls with no evidence of Axis I disorders as determined by the SCID-NP were recruited through advertisements at ZHH. All participants were between the ages of 18 and 65 years.

Exclusion criteria for all participants included: 1) history of CNS trauma, neurological disorder, and attention deficit hyperactivity disorder (ADHD) or a Learning Disability diagnosed in childhood; 2) diagnosis of recent substance abuse/dependence (past 3 months); 3) active, unstable medical problem; and 4) ECT in the past 12 months. In addition, healthy controls were excluded if they met criteria for an Axis I disorder as determined by the SCID-NP or if they reported a history of a diagnosed Axis I disorder in any first degree relatives. All procedures were approved by the local IRB and written informed consent was obtained from all participants.

2.2. Materials

Affective temperaments were assessed using the TEMPS-A (Akiskal et al., 2005), a 143-item self-report questionnaire that results in scores on five temperamental subscales: cyclothymic, depressive, anxious, hyperthymic, and irritable.

Neurocognitive performance was evaluated using the MATRICS Consensus Cognitive Battery (MCCB) (Nuechterlein and Green, 2006). The MCCB is composed of tests that give rise to the following 7 cognitive domains: 1) processing speed (assessed by the Brief Assessment of Cognition in Schizophrenia (BACS) and Trail Making Test part A); 2) attention (assessed by the Continuous Performance Test—Identical Pairs (CPT-IP); 3) working memory (measured by the Wechsler Memory Scale [spatial and letter-number span]); 4) verbal learning (using the Hopkins Verbal Learning Test—Revised [HVLT-R]); 5) visual learning (as assessed using the Brief Visuospatial Memory Test—Revised [BVMT-R]); 6) reasoning and problem solving (as assessed by the Neuropsychological Assessment Battery [NAB] Mazes subtest); and 7) social cognition (as measured by the Mayer–Salovey–Caruso Emotional Intelligence Test [MSCEIT[).

2.3. Analytic approach

Patients with BD and HCs were first compared in terms of demographic characteristics (age, sex and race), clinical features (manic and depressive symptoms as measured by the CARS-M and by the HRSD), affective temperaments, and neurocognitive functioning (as measured by the cognitive domains from the MCCB, as well as premorbid IQ) using Chi-square and independent sample *t*-tests as appropriate.

To evaluate whether affective temperaments were related to current sub-threshold mood symptoms, bivariate correlations were calculated between the five TEMPS-A subscales and depressive and manic symptoms (HRSD and CARS-M scores, respectively). Partial correlation analyses were used to test the association between the TEMPS-A subscales and cognitive domains in the whole sample using HRSD, CARS-M and WRAT-3 (premorbid IQ) scores as covariates; the same analysis was then conducted in the two samples of BD and HC subjects separately. The False Discovery Rate (FDR) was applied to control for type I error due to multiple comparisons.

3. Results

The sample was comprised of 64 patients with BD and 109 with HCs. Among BD patients, the majority (77%; $n=49$) had a diagnosis of BD I, 14% ($n=9$) had a diagnosis of BPD II and 9.4% ($n=6$) had a diagnosis of BD NOS. No statistically significant differences were detected between patients and healthy controls in terms of sex, race, age and premorbid IQ (Table 1). Although affectively stable at the time of assessment, BD patients scored significantly higher