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Research report

Principal domains of quantitative anxiety trait in subjects with lifetime history of mania

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ABSTRACT

Background: High comorbidity rates for anxiety have been documented in subjects with history of mania or hypomania. We explored the presence of latent constructs of quantitative anxiety in subjects who have a history of mania or hypomania.
Methods: We conducted an exploratory factor analysis of anxiety trait in 212 subjects who have a lifetime history of at least one manic/hypomanic syndrome. Participants were originally recruited for a Costa Rican sibling pair genetic study of Bipolar Disorder. We used principal factors extraction method with squared multiple correlations (SAS/SAT Professional software) of the STAI (trait subscale).
Results: A three-factor solution with a good simple structure and statistical adequacy was obtained with a KMO of 0.84 (>0.6) and Bartlett's Test of Sphericity of 2.4668E-162 ($p<0.05$). Items were grouped into anxiety-absent factor and the anxiety-present symptoms in two additional factors based on the nature of the symptoms, worry and rumination.
Limitations: Comorbid disorders could affect the interaction of anxiety score with manic/hypomanic symptoms. Some statistical parameters (mood status independence, score distribution and correlation between trait score and quantitative mania/hypomania) were not taken into consideration to extract the factors. Because anxiety dimensions were explored on individuals with history of mania or hypomania and not in healthy subjects, comparison of our results with other studies can draw confusing conclusions.
Conclusions: Two underlying constructs, worry and rumination may explain anxiety sub-syndromic symptoms in Costa Rican patients with history of mania or hypomania.
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1. Introduction

Current diagnostic systems do not adequately reflect the complexity of bipolar disorder (BD) (Akiskal et al., 2000; Akiskal and Pinto, 1999). Categorical diagnosis and global severity assessments provide suboptimal information to improve our knowledge on pathophysiology, diagnostic assessment, prognosis, and novel therapies. Insights into BP genetics, illness course and pharmacological studies increasingly reinforce this conclusion. Syndromal diagnostic criteria could also be aided by the reliable convergence of several dimensional variables, including behavioral domains, illness course and family history (Contreras et al., 2010; Goodwin and Jamison, 2007; Vieta and Phillips, 2007).

High comorbidity rates for anxiety have been documented in bipolar I disorder (MacKinnon et al., 2002; McElroy et al., 2001). However, sub-syndromal levels of anxiety have also been associated with bipolar I patients who did not meet criteria for a categorical Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) anxiety disorder (Mantere et al., 2008). Research on the underlying variables and factors is limited to individual categorical clinical states (Sato et al., 2002). The above limitations have made it difficult to

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extrapolate results to current clinical practices and to replicate findings.

Clinical and epidemiologic evidence suggests that major mood disorders form a spectrum from major depressive disorder to pure mania (Angst et al., 2010). More specifically, transient manic symptoms in children were probed to be a risk factor for eventual conversion to the bipolar spectrum disorder (Nadkarni and Fristad, 2010). Family studies have also supported the concept of a spectrum of subthreshold affective traits or temperaments (e.g. cyclothymia and anxiety) in bipolar pedigrees (Vázquez et al., 2008). Since the concept of bipolar spectrum denotes overlapping clinical expressions, without necessarily implying underlying genetic homogeneity; we arbitrarily defined bipolar spectrum disorder as lifetime history of any manic syndrome/episode. Thus, we analyzed subjects who have a history of mania or hypomania (bipolar disorder type I, bipolar disorder type II, bipolar disorder not otherwise specified, schizoaffective bipolar disorder, schizophrenia with manic syndrome and substance related manic syndrome). One of the reasons for using any manic or hypomanic syndrome as inclusion criteria is the fact that in our previous published work the trait score was correlated with lifetime mania (LDPS M-1 duration × severity) ($p<.0001$) after controlling for age and gender. In that study we did not find significant correlation between anxiety trait and depression (Contreras et al., 2010).

The goal of this study was to explore the presence of latent constructs which contribute to the STAI score in subjects who have a history of mania. We used the anxiety trait (trait subscale of the STAI) that showed normal distribution in healthy subjects, significant heritability and genetic correlation and independence to mood clinical state in our multiplex bipolar I families (Contreras et al., 2010). Also, research has shown that state–trait dimensions (from studying the two subscales together) may be multidimensional themselves (Virella et al., 1994). The advantage of knowing if there are factors is to better understand the biologic components which make up the global STAI score in this group of patients. If this anxiety trait represents a biological marker for bipolar I disorder in this Costa Rican sample, exploration of its underlying constructs might provide a high face and construct validity with respect to mania/hypomania in this Costa Rican sample.

We reasoned that the combination of quantitative anxiety trait and best estimation diagnostic process based on DSM-IV diagnostic criteria would serve to yield reliable and informative scores on fundamental affect components of subjects with history of mania/hypomania.

2. Methods

2.1. Participants

Subjects were originally recruited for a multi-site bipolar sibling pair study (Genetics of Bipolar disorder in Latino Populations NIMH 1 R01 MH069856-01A2). The study was explained to each subject and written informed consent was obtained. This study was reviewed and approved by the Institutional Review Boards of the University of Costa Rica and the University of Texas (UTHSCSA). The sample was composed of 212 subjects. Each individual had lifetime history of at least one manic/hypomanic syndrome.

2.2. Diagnostic assessment

The subjects were diagnosed based on the diagnostic criteria of DSM-IV through a best estimation process utilizing clinical information obtained from the Diagnostic Interview for Genetic Studies (Nurnberger et al., 1994), a Family Interview for Genetic Studies (Maxwell, 1992) and psychiatric records. Final diagnoses were determined through a consensus process where two independent psychiatrists reviewed all available information and arrived at independent diagnoses.

2.3. Anxiety assessment

Sub-syndromal anxiety was assessed by means of the STAI to measure anxiety scores in each individual. The STAI is a self-rated instrument that contains two 20-item scales (4 response choices per item, higher scores indicate higher anxiety) (Spielberger et al., 1983). One scale measures state anxiety (i.e. the extent to which respondents experience anxiety symptoms at the time of measurement) (Vigneau and Cormier, 2008). The second scale measures trait anxiety (i.e. the extent to which respondents generally experience anxiety symptoms). This instrument has been validated in Spanish (Rodrigo and Lusiardo, 1988).

2.4. Exploratory factor analysis

Exploratory factor analysis was performed using the principal factors extraction method with squared multiple correlations (SMC) of each variable with all the other variables for the prior communality estimates. This is the simplest and computationally most efficient method of common factor analysis. Although maximum likelihood (ML) factor analysis has desirable asymptotic properties and allows to test hypotheses about the number of common factors, it generates better estimates in samples larger than the number of subject of the current study (Joreskog, 1977).

To determine whether the common factor model is appropriate, we calculated the Kaiser's measure of sampling adequacy (KMO). This measure varies between 0 and 1; a value greater than 0.6 was considered the minimum accepted value (Kaiser, 1974). Bartlett's Test of Sphericity tests the null hypothesis: that the correlation matrix is an identity matrix (matrix in which all of the diagonal elements are 1 and all of diagonal elements are 0). By using the test, the null hypothesis would be rejected.

Partial correlation (controlling all other variables) was explored to evaluate whether the data was appropriate for the factor model. It is presumed that partial correlation will be small compared to the original correlations. SMC replaces the diagonal of the original observed correlation matrix by these square multiple correlations.

During the extraction, the values indicate the proportion of each variable's variance that can be explained by the retained factors. Variables with high values are well represented in the common factor space, while variables with low values are not well represented. Because the square multiple correlations are usually less than one, the resulting correlation matrix for factoring is called the reduced correlation matrix. The Regression Method was used to produce the coefficients for each item in order to generate the estimated