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Underlying domains of anxiety trait in a Costa Rican sample: preliminary results

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Abstract

Background: Imprecision of the psychiatric phenotype might partially explain the failure of genetic research to identify genes that contribute to susceptibility of anxiety disorders. Previous research concluded two underlying constructs, worry and rumination, might explain anxiety sub-syndromic symptoms in Costa Rican patients with history of mania. The goal of the current study is to explore the presence of latent constructs for quantitative anxiety in a group of subjects with a wide diagnostic phenotype and non-affected individuals.

Methods: We conducted an exploratory factor analysis of anxiety trait in 709 subjects. Our sample was comprised by 419 subjects with psychiatric disorders and 290 non-affected individuals. We used principal factors extraction method with squared multiple correlations of the STAI (trait subscale).

Results: We found the following preliminary results: a three-factor solution with a good simple structure and statistical adequacy was obtained with a KMO of 0.92 (>0.6) and Bartlett's Test of Sphericity of 5644,44 ($p<0.05$). The STAI items were grouped into three factors: anxiety-absent, worry and rumination based on the characteristics of the symptoms.

Conclusion: Two underlying constructs, worry and rumination may explain anxiety sub-syndromic symptoms in Costa Rican subjects. Our proposed underlying structure of subsyndromal anxiety in individuals should be considered as an important factor in defining better phenotypic characterizations on a broader diagnostic concept. Worry and rumination as a phenotypic characterization may assist in genotyping; however, its predictive value on actual illness outcome still requires more research. The Genome-Wide QTL analysis for anxiety trait in the same sample is ongoing.

Declarations of interest: none

Conflict of interest
None of the authors have financial disclosures.

Introduction

Anxiety is one of the most prevalent psychiatric complaints in the general population, and plays a very important role in many theories of personality and psychopathology (Oei, Evans & Crook, 1990; Kessler, Ruscio, Shear & Wittchen, 2010). According to the current diagnostic classification, it can be classified into several groups such as separation anxiety disorder, selective mutism, specific phobia, social anxiety disorder, panic disorder, agoraphobia and generalized anxiety disorder (Wittchen et al., 2011). Epidemiological studies have shown that anxiety disorders are more frequent than mood disorders and substance use disorders (Demyttenaere et al., 2004; Kessler et al., 2010). There are many factors affecting the occurrence of anxiety disorders, including gender and age (Kessler et al., 2010; Canuto et al., 2017), socioeconomic disadvantage (Moffitt et al., 2007; Kawakami et al., 2012), difficult interpersonal relationships (Beesdo, Pine, Lieb & Wittchen, 2010), urbanicity (Prina, Ferri, Guerra, Brayne, & Prince, 2011) and violence (Stein et al., 2009).

Information about the prevalence of anxiety disorders is highly variable and fragmented due to methodological differences among studies (Somers, Goldner, Waraich, & Hsu, 2006; Tanios et al., 2009). This is evident in the estimates on the global prevalence of anxiety disorders, which range between 0.9% and 28.3% (Baxter, Scott, Vos & Whiteford, 2013). In the same way, imprecision in the clinical diagnosis also contributes to this variation, because the subjects who present anxiety do not always meet all criteria for a full-blown disorder (Contreras, Hare, Pacheco, Escamilla & Raventos, 2010). As an additional complication factor, comorbidity between disorders is common, for example, bipolar disorder or schizophrenia with anxiety (McElroy et al., 2001; MacKinnon et al., 2002; Braga, Mendlowicz, Marrocos & Figueira, 2005; Braga, Reynolds & Siris, 2013).

Although the Diagnostic and Statistical Manual of Mental Di orders, Fifth Edition (DSM- 5) specifies the criteria used for diagnosis in the clinical practice (Mantere, Suominen, Valtonen, Arvilommi & Isometsä, 2008), in research other clinical assessment instruments are usually added. The State-Trait Anxiety Inventory (STAI) (Spielbeger, Gorsuch, Lushene, Vagg & Jacobs, 1983) is the most commonly used instrument to study anxiety. The STAI scale consists of two sub-scales. The first (anxiety trait), includes items related to personality traits, which rate individual differences in threatening situations (i.e. the extent to which respondents generally experience anxiety symptoms) and the second (anxiety state), consists of items that refer to a transient period with tension and an increase in autonomic nervous system activity, due to environmental factors that may or may not generate anxiety (i.e. the extent to which respondents experience anxiety symptoms at the time of measurement) (Spielberger et al., 1983).

In Costa Rica, the STAI scale has been used in the study of sub-syndromic anxiety. Previous research has focused on the latent constructs of quantitative anxiety trait in subjects who have a history of mania or hypomania, but not in non-affected individuals. Contreras et al. (2012) found that two underlying constructs, worry and rumination might explain anxiety sub-syndromic symptoms. Their findings could contribute to a better phenotypic definition of this complex psychopathology. However, because our interest is to point out the role of the normal anxiety and therefore, to identify possible differences in the genetic signals

associated with both underlying constructs, the first step is to replicate the initial findings with a sample that also includes non-affected individuals. Hence, the objective is to explore the presence of latent constructs in a quantitative anxiety trait in a larger sample than the preliminary study, including non-affected individuals.

Methods

-Participants:

Subjects were originally recruited for a multi-site bipolar sib-pair study (Genetics of Bipolar disorder in Latino Populations NIMH R01 MH069856–01A2). This study was reviewed and approved by the Institutional Review Board of the University of Costa Rica. The study was explained to each subject and written informed consent was obtained. The sample consists of 709 individuals, and includes subjects with a diagnosis of a wide range of psychiatric disorders (schizophrenia, schizoaffective disorder, bipolar disorder and major depressive disorder), as well as non-affected individuals.

-Diagnostic assessment:

The participants were diagnosed based on the diagnostic criteria of DSM-IV through a best estimation process. Psychiatric records, clinical information obtained from the Diagnostic Interview for Genetic Studies (Nurnberger et al., 1994) and a Family Interview for Genetic Studies (Maxwell, 1992) were used for this purpose. Final diagnoses were determined through a best estimate process where first two psychiatrists arrived to independent diagnoses after reviewing all available information and then a consensus diagnosis.

-State-Trait Anxiety Inventory (STAI):

Sub-syndromal anxiety was assessed by mean of the STAI to measure anxiety scores in each individual. The STAI is a self-rated instrument that consists of two 20-items sub-scales. Respondents reported their choice for each item in a scale of 4 points, ranging from 0 (almost never) to 3 (almost always); higher scores indicate higher anxiety (Spielberger et al., 1983). This instrument has been validated in Spanish (Rodrigo & Lusiardo, 1988). In the previous study the results of state anxiety show d variation depending clinical status of the subject, at the time of anxiety assessment. Participants with a psychotic or affective episode showed more anxiety than euthymic subjects. Anxiety trait was independent of the clinical status (Contreras et al., 2010). For that reason the purpose of this study was to analyze only anxiety trait.

Exploratory factor analysis:

We calculated the Kaiser’s measure (KMO) of sampling adequacy and Bartlett’s Test of Sphericity to determine whether the common factor model is appropriate to this specific data set. This measure varies between 0 and 1, a value greater than 0.6 was considered the minimum accepted value (Kaiser, 1960). 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. Squared multiple correlations method (SMC) replaces the diagonal of the original observed correlation matrix by these square multiple correlations.

The exploratory factor analysis was performed using the principal factors extraction method with 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 subjects of the current study (Joreskog, 1977).

Extraction method and optimal number of factors:

The method of extraction was the ML and varimax rotation. During the extraction, the values indicate the proportion of each variable's variance that can be explained by the retained factors. The initial eigenvalues are the variances of the factors. To determine the optimal number of factors to be extracted, the protocol required each factor to have at least four items with rotated factor loading scores greater than 0.30. This cut-off score was chosen because it does not eliminate potentially significant factors and it conforms to traditional exploratory factor analysis methodology (Floyd & Widaman, 1995).

The screen plot (not shown) produces a plot of the eigenvalues that is helpful in deciding how many factors to use (Fabrigar, Wegener, MacCallum & Strahan, 1999).

Results

Sample characteristics

Our sample was comprised by 419 (59%) subjects with psychiatric disorders and 290 (41%) non-affected individuals. The most frequent diagnoses were bipolar disorder, 167 (23%) followed by major depressive disorder, 144 (20%). The sample was 57% female and had a mean age of 41.2 (SD 14.90).

Factor structure

The correlation matrix of STAI trait subscale (20 items) was computed before the analysis, to evaluate if the common factor model was appropriate for our sample. Inspection of the correlation matrix showed that the correlations were substantial, indicating the presence of a substantial general factor. KMO of 0.92 (>0.6) and Bartlett's Test of Sphericity of 5644.44 ($p<0.05$) showed adequacy of data for factor analysis. After the factorial analysis, according to the proportion criterion (>0.30) and the scree plot, three factors can be retained (Table 1). Based on the obtained factor pattern all variables except items 25 and 34 had high loadings on one factor and became easier to interpret after rotation. As seen in Table 1 19 items had factor loadings ranging from 0.44 to 0.80. The analyses identified tree factors according to the grouping of items. The first included items of absence of anxious symptoms, explaining a 20.4% of the total variance. Factors 2 and 3 consist of items related to the presence of anxiety. Factor 2 explains 19.2% and factor 3 explains 13.8% of the total variance. All three factors together explain 53.4% of the total variance.

Discussion

This study presents an analysis of the STAI in a sample that includes subjects from families with high prevalence of psychiatric disorders. Population-based analyses are beyond the scope of the current work and therefore caution should be taken before drawing substantive conclusions. The exploratory factor analysis generated three different groups of items. Responses to items associated with factor 1 describes absence of anxiety. The items associated with factor 2 indicate anxiety about actual and future events and stressful situations. On the other hand, factor 3 clusters components associated with thoughts about past events and recurrent situations. Based on the characteristics of each group of items, the following labels were given: anxiety-absent, worry, and rumination, respectively.

The exploratory factor analysis suggested that a three-factor solution was the best fit for this data set. These constructs are consistent with several previous studies. One of them analyzed the STAI factorization in a sample of patients diagnosed with depression; three underlying factors were identified in the exploratory factor analysis: state anxiety, positive trait anxiety, and negative trait anxiety (Guillén-Riquelme & Buela-Casal, 2015).

In another study about stress, Barker, Barker & Wadsworth Jr (1977) administered the STAI to students in two different moments and found three factors: one associated to anxiety state (Factor I) and two related to anxiety trait (Factors II and III). In that research, the objective was to test the stability of anxiety state and anxiety trait sub-scales (40 items) in students during two different occasions.

In our current study, we used only the anxiety trait (20 items) subscale, which was measured once in individuals with psychiatric disorders and non-affected subjects. Our study and the results of Barker and collaborators, identified two underlying factors related to anxiety trait. Barker described that factor II focuses on feelings and reflects the individuals' selfperceived levels of general anxiety while factor III describes the kind of person they see themselves (Barker et al., 1977). In the present study, we defined factors as referring to past or recurrent and future events.

To understand anxiety disorders, it is important to point out the role of the normal anxiety response. This can be understood from an evolutionary point of view, since anxiety is one of the most common evolutionarily conserved emotions (Brüne, 2016). In evolution, anxiety has provided an adaptive advantage because it protects the individual from potential threats and danger in response to cues (Marks & Nesse, 1994). That is, from the point of view of survival, worrying, planning, and investing time in thinking about potentially threats could be considered an advantage (Bateson, Brilot & Nettle 2011). However, acceding to epidemiological studies, long-term survival rate is greater in individuals with lower anxiety (Lee, Wadsworth & Hotopf, 2006; Mykletun, Bjerkeset, Overland, Prince, Dewey & Stewart, 2009).

The apparent contradiction between the evolutionary adaptive advantage hypothesis and the epidemiological studies could be explained as a difference in anxiety intensity. Anticipatory cognitive processes have an adaptive function when they are executed at a commensurate level with the likelihood and severity of the threat, but can be maladaptive when conducted

in an excessive manner (Rosen & Schulkin, 1998; Grupe & Nitschke, 2013). It is not clear if anxiety is under the force of evolution because it is not well established if the presence of anxiety in patients necessary aff cts biological fitness (Mykletun, Bjerkeset, Øverland, Prince, Dewey & Stewart, 2009). It could also be explained if the anxiety construct is heterogeneous and includes different biological responses, some advantageous for survival and some not, which is our present hypothesis. If some aspects of the anxiety trait have been selected for in the course of evolution, genetic markers related to the trait can potentially be found. We will evaluate this hypothesis as a second step.

Finally, the expression of anxiety symptoms is subject to cultural variation and cultural norms. It is necessary o ha e more research data of manifestation of anxiety traits among different cultures. Most. of the current research focus on DSM system categories such as generalized anxiety disorder or social phobia with few studies on anxiety traits and its distribution in the general population. Further research must include the factor structure of anxiety in other Latino populations so that our results can be compared with other populations. A recommended approach is to control for potential ecological effects on anxiety traits by including specific environmental factors. On the other hand, we also considered as a limitation, that is important to remark that this is an exploratory factor analysis of subjects who have history of mania / hypomania and non-affected without taking into consideration familiarity.

In conclusion, our preliminary results showed two underlying constructs, worry and rumination, that may explain anxiety sub-syndromic symptoms. These underlying constructs could improve phenotypic characterization, both for genetic mapping purposes, and to study their possible predictive value on disease prognosis. The next step of our research is to identify quantitative trait loci (QTL) related to anxiety in this sample.

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Highlights

- STAI trait subscale items grouped into three factors: no anxiety, worry and rumination
- Two underlying constructs, worry and rumination may explain anxiety sub-syndromic symptoms.
- This underlying contracts are present in subjects with psychiatric diagnosis and not affected individuals.
- The underlying constructs could improve phenotypic characterization, both for genetic mapping purposes, and to study their possible predictive value on disease prognosis.

Table 1:

Factors loadings (exploratory varimax factor analysis)

Anxiety Symptoms	Factor 1 (Anxiety-absent)	Factor 2 (Worry)	Factor 3 (Rumination)
I am calm and cool	0.743		
I feel secure	0.723		
I am happy	0.722		
I am content	0.716		
I feel rested	0.715		
I feel pleasant	0.702		
I am a steady person	0.647		
I feel like crying		0.803	
I worry too much over something that really doesn't matter		0.787	
I tire quickly		0.777	
I get in a state of tension or turmoil as I think over my recent concerns and interests		0.708	
I don't usually confront difficulties		0.442	
I wish I could be as happy as others seem to be			0.692
I take disappointments so keenly that I can't put them out of my mind			0.653
I feel that difficulties are piling up so that I cannot overcome them			0.611
Some unimportat thought runs through my mind and bothers me			0.592
I lack self-confidence			0.557
I feel inadequate			0.527
I usually take things too seriously			0.525

Note: Only values greater than 0.30