Manuscript Details

Manuscript number	JAD_2018_2462_R1
Title	Spanish validation of the Barcelona TEMPS-A questionnaire in patients with bipolar disorder and general population
Article type	Research Paper

Abstract

Background: The Temperament Evaluation of the Memphis, Pisa, Paris, and San Diego (TEMPS-A) is a self-administered questionnaire intended to assess five affective temperaments: depressive, cyclothymic, hyperthymic, irritable and anxious. Our objective was to examine the psychometric properties of the TEMPS-A using a sample comprised by patients with bipolar disorder (BD) and healthy controls (HC) and to determine cut-off scores for each temperament. Methods: Five hundred and ninety-eight individuals (327 BD and 271 HC) completed the TEMPS-A. Cronbach's alpha was used to examine internal consistency reliability. Test-retest reliability and association between different temperamental scales were assessed using Spearman correlation. To confirm factor structure a confirmatory factor analysis (CFA) was carried out. Cut-off scores indicating the presence of dominant temperament were also calculated. Results: Internal consistency was optimal for all temperament subscales (α: 0.682- 0.893). The questionnaire demonstrated good test-retest reliability (ρ: 0.594- 0.754). The strongest positive associations were found between cyclothymic and anxious and between depressive and anxious temperaments. Hyperthymic and depressive as well as hyperthymic and anxious temperaments showed a strong negative correlation. Limitations: The HC sample was not matched with the BD group. There were some sociodemographic and clinical differences between groups that may impact on the obtained results. A portion of patients with BD was recruited from tertiary centers. Conclusions: The Spanish version of the Barcelona TEMPS-A questionnaire presents a good internal consistency and their results are stable in clinical population. The performance of the Barcelona TEMPS-A is as good as the original scale.

Keywords	TEMPS-A; validation; psychometric properties; Spanish; bipolar disorder: non-clinical population; temperament.

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Suggested reviewers	Gustavo Vazquez, Zoltan Rihmer, Xenia Gonda, Konstantinos Fountoulakis

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November 26th, 2018

Dear Editor-in-Chief
Prof. Paolo Brambilla,

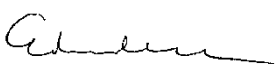
Please find enclosed our manuscript entitled "**Spanish validation of the Barcelona TEMPS-A questionnaire in patients with bipolar disorder and general population"** to be considered for publication in "Journal of Affective Disorders", as an original article if you find it suitable.

Affective temperaments may be considered as subclinical manifestations of affective disorder. In this sense, the Temperament Evaluation of the Memphis, Pisa, Paris, and San Diego (TEMPS-A) questionnaire is considered as the gold-standard instrument to assess affective temperaments in both general population and psychiatric patients. However, most of studies have so far assessed its psychometric properties using non-clinical samples. The present work was aimed to analyse the internal consistency and test-retest reliability, as well as to examine its factor structure of the Barcelona TEMPS-A (Sanchez-Moreno et al., 2005) in a large non-clinical and clinical Spanish population consisting of patients with BD. We also were aimed to provide preliminary cut-off scores for each subscale in both populations. Our results indicate that the Spanish version of the Barcelona TEMPS-A questionnaire presents a good internal consistency and their results remain stable over time in clinical population.

The present manuscript represents original material and has not been previously published, is not being considered for publication elsewhere and has been approved by each author. Moreover, all forms of conflict of interest by all authors were clearly identified in the text.

We hope this manuscript will be of your interest.

Sincerely,



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January 16th 2019

Dear Editor-in-Chief, Professor Soares,

Thank you for considering our manuscript Ref: JAD_2018_2462 entitled "SPANISH VALIDATION OF THE BARCELONA TEMPS-A QUESTIONNAIRE IN PATIENTS WITH BIPOLAR DISORDER AND GENERAL POPULATION" for further revision in Journal od Affective Disorders. We are grateful to the reviewers for their effort and comments and we appreciate that many of the changes that they suggested have contributed to improve our manuscript. We have adjusted the text according to their suggestions, as appropriate, and the changes appear detailed below in response to each of the reviewer's comments.
Please find our responses in blue lettering. We hope that the current version of the paper will be suitable for publication in your journal.

Reviewers' comments:

Reviewer 1

1. In the Introduction the authors write:
"Noteworthy, evidence suggest that specific temperaments have potential negative clinical implications in patients with bipolar disorder (BD), such as a worse prognosis (Perugi et al., 2012), a higher rate of comorbidity (Rybakowski et al., 2014) and suicidal behavior (Baldessarini et al.,2016;Jimenez et al., 2016;Rihmer et al., 2009;Tondo et al., 2018), a poorer drug response (de Aguiar et al., 2014;Rybakowski et al., 2013) and lower adherence (Solmi et al., 2016), amongst others"

In addition to this, I suggest to mention that in addition to this, specific affective temperaments have also specific impact on smoking habits and on cardiovascular morbidity in psychiatrically healthy persons (Eory et al, Psychother Psychosom 2014, 83: 187-189. Eöry et al, J Affect Disord, 2015; 172: 397-402. Nemcsik et al, J Psychosom Res, 2017; 103: 108-112).

We appreciate this point and, as suggested by the reviewer, some comments concerning the abovementioned works have been added in the "Introduction" section. Now it is stated: ***"It is noteworthy that some specific affective temperaments have been also found to impact on smoking habits and on cardiovascular morbidity in***

psychiatrically healthy individuals (Eory et al., 2014;Eory et al., 2015;Nemcsik et al., 2017)" (see page 4, 2nd paragraph).

2. Also on the same place:
"This self-administered questionnaire has been widely translated and validated across different countries in multiple languages, becoming a key tool for measuring affective temperaments in the scientific community (Akiskal et al., 2005a,b)".

I suggest to quote also Gonda et al, J Afect Disord, 2011; 131: 45-51. This is more recent and comprehensive.

We agree with reviewer 1 and following his/her advice we have added the aforementioned reference.

3. In Methods section:
"Additionally, a history of mental illness and previous or current use of prescribed psychotropic drugs were considered as exclusion criteria for the healthy control participants".

It is Ok, but no clinical interview/screening has been performed to reject persons with undiagnosed mental illness?

We appreciate this comment very much, since we have realized that this matter was not really accurately described in the submitted manuscript. Actually, all healthy volunteers were screened not only for personal history of any psychiatric condition or current use of psychiatric medication, but also for the existence of any psychiatric illness among their first-degree relatives. So now we have included a more detailed description of this procedure in order to avoid misunderstanding. Now it is stated: ***"...All healthy volunteers were also screened for personal and family history of any psychiatric condition. Therefore, a history of mental illness and previous or current use of prescribed psychotropic drugs were considered as exclusion criteria for the healthy control participants. Additionally, all those healthy controls reporting to have a first-degree relative with any psychiatric condition were also excluded from the study."*** (see page 6, 2nd paragraph).

The authors also shoud note that HC group is not representative for the Catalonian population.

This validation study was not only limited to Catalonian population but is intended to be a general Spanish population validation. In fact, as reported in the "Methods" section our healthy volunteers were recruited from two different sites in Spain, one group from Barcelona and other from Granada, in order to enhance generalization of our results.

4. In the Discussion:
"On the contrary, the high prevalence of the hyperthymic temperament in

HC surprises as several prior works reported very low rates of the hyperthymic dominant temperament across non clinical population (Vazquez et al., 2007; Fountoulakis et al., 2014; Karam et al., 2005; Lin et al., 2013; Placidi et al., 1998)."

BUT: Rózsa et al (J Affect Dsiord, 2008; 106; 45-53) have reported that the dominant hyperthymic temperament (= z + 2SD or above) in a normative sample of Hungary was 3,0% (males: 5,4, Females: 2.0%) while the same rate of dominant depressive temperament were 3,2% (males: 2,7%, females: 3,4%).

Thank you for this comment. We have added a comment concerning this work in the "Discussion" section. Now it is stated: ***"... However, it should be mentioned that Rosza and colleagues reported that rates of dominant hyperthymic temperament were mainly as high as depressive in a large sample of healthy volunteers. Moreover, when rates between genders were compared, the hyperthymic was one of the most prevalent dominant temperaments among men, only surpassed by cyclothymic (Rozsa et al., 2008.)"*** (see page 12, last paragraph).

Reviewer3

The present paper is an important and accurate description of the validation of the TEMPS-A in Spanish, both on healthy in clinical samples and also attempting to establish a cutoff score which enhances the clinical utility of the scale.
While the study is well designed and executed and the paper is well-written, I have a few suggestions:

1. Some of the highlights appear to be too long.

Thank you for this suggestion. Following the reviewer's recommendation, we have shortened the highlights.

2. Title and abstract: the title refers to Barcelona TEMPS-A and the abstract and elsewhere the instrument is referred to interchanging either as TEMPS-A or as Barcelona TEMPS-A. This should be clarified.

Following this advice we have homogenized the wording along the manuscript when we refer to the Barcelona version of the TEMPS-A.

Also, are there any differences between the Spanish and original version of the TEMPS-A besides the language: For example the Munster TEMPS-A is a shorter version?

Originally, the first version of the TEMPS-A comprised 84 items, assessing four different temperaments: dysthymic, cyclothymic, hyperthymic and irritable. Afterwards, and prompted by clinical and theoretical considerations, 26 new items assessing the anxious temperament were added, resulting in what has been considered as the definitive structure of this questionnaire (110 items assessing five temperaments) (Akiskal HS et al. (2005) J Affective Disord. 85, 45-52). The Spanish

version of the Barcelona TEMPS-A was adapted from the latter questionnaire, which, in term, has been the one which has been translated and validated in several countries around the world. It should be remarked that the Barcelona TEMPS-A was obtained by the application of the recommended methodology for the cultural and semantic adaptation of health measurement tools (Sánchez-Moreno et al. (2005) Actas Esp. Psiquiatr. 33, 325-330).

Therefore, there are no remarkable differences between our version and the TEMPS-A.

3. Introduction: while concise and focused, it should be a bit more comprehensive. For example other temperamental models could be mentioned in one sentence indicating that while there are several models of temperament they are more used to describe the healthy personality with TEMPS model being the one that is specific to also encompass affective disorders.

As suggested by reviewer 1, we have added a comment concerning this recommendation in the "Introduction" section. Now it is stated: ***"...This questionnaire differs from other scales based in other temperamental models more used to describe healthy personality, such as the Cloninger's model (Cloninger et al., 1993) and the Five Factor Model (Costa et al., 1985). In this sense, the TEMPS-A taps subaffective trait expression and frames questions in the language of affectivity (Akiskal et al., 2005b; Rozsa et al., 2008). Therefore, this instrument covers more specifically the temperamental assessment in people with affective disorders"***. (see page 4, 1st paragraph).

Also, the validation and different versions of TEMPS in other languages could also be reviewed in one sentence.

Following this reviewer's suggestion we added the requested information in the "Introduction" section. Now it is stated: ***"...This self-administered questionnaire has been translated and validated in several languages, including Spanish (Sanchez-Moreno et al., 2007; Vazquez et al., 2007), American English (Akiskal et al., 2005b), French (Akiskal et al., 2005a), Portuguese (Figueira et al., 2008;Woodruff et al., 2011), Italian (Pompili et al., 2008), German (Bloink et al., 2005), Polish (Borkowska et al., 2010), Serbian (Ristic-Ignjatovic et al., 2014; Hinic et al., 2013), Hungarian (Rozsa et al., 2008), Greek (Fountoulakis et al., 2014), Turkish (Vahip et al., 2005) , Arabic (Karam et al., 2005), Mandarin (Lin et al., 2013), and Japanese (Matsumoto et al., 2005), becoming a key tool for measuring affective temperaments in the scientific community (Akiskal et al., 2005b,c; Gonda et al., 2011). It should be remarked that different short forms of this questionnaire are also available in different languages (Akiskal et al., 2005c; Erfurth et al., 2005; (Erfurth et al., 2005;Krebs et al., 2006;Nakato et al., 2016;Preti et al., 2010;Yuan et al., 2015)."*** (see page 5, 1st paragraph).

4. Aims: from the aims it is not easy to find out what cut-off scores would mean: cut off for the healthy controls vs bipolar?

Following this reviewer's advice, we have rewritten this secondary aim. Now it is stated: ***"A secondary purpose was to determine the prevalence of the Barcelona TEMPS-A dominant temperaments amongst Spanish population by means of preliminary cut-off scores for each temperament calculated on the one hand for the whole sample, and on the other for bipolar population and healthy controls, separately."*** (see page 5, 2nd paragraph).

5. Methods: The sample size and especially the healthy sample size is too small for a validation study. Generally for a good FA you need 4 times as many subjects as items in the instrument. This should be mentioned as a limitation.

We appreciate this comment very much. However, we would like to point out that both internal consistency tests and CFA analysis were actually carried out using data from the whole sample (including patients with bipolar disorder and healthy controls) consisting of 598 individuals, exceeding the *a priori* recommended sample size to perform this sort of analysis (n > 440). We consider, therefore, that conditions to ensure the quality of the results are guaranteed in our work.

6. Methods: what was the reason for not including UD patients?

So far, most of the TEMPS-A validation studies were mainly focused on general population, for that reason, our main aim was to focus our validation study on a sample including patients with bipolar disorder. In this sense, our goals were to explore potential discrete temperamental profiles and to determine different cut-off scores regarding different subscales between groups. We consider that this issue may be relevant from a clinical perspective since it would enhance accurate diagnosis of this group of affective patients. Of course, the inclusion of patients with unipolar depression would be desirable since it would enhance a clear depiction of differences among temperamental profiles between both affective conditions. Unfortunately, a sample of unipolar depressive patients was not available when this study was designed and conducted.

7. Given the known biological and genetic basis of temperaments, was there any screening for affective disorders in the family and first degree relatives? This is also especially important if the sample is young and may not have developed an affective disorder yet while already carrying the temperamental disposition for it. Please add this to the limitation.

*(Please, see also response to third query by Reviewer 1)

This was indeed unexpectedly missing, so now we have included a more detailed description of exclusion criteria concerning the presence of family history of any psychiatric condition among the healthy control group. Now it is stated: ***"…All healthy volunteers were also screened for personal and family history of any psychiatric***

condition. Therefore, a history of mental illness and previous or current use of prescribed psychotropic drugs were considered as exclusion criteria for the healthy control participants. Additionally, all those healthy controls reporting to have a first-degree relative with any psychiatric condition were also excluded from the study.” (see page 6, 2nd paragraph).

8. Was the bipolar sample taking medications? I suppose yes and this of course cannot be avoided with a clinical sample. Also, add it to the limitations that this may influence the experience of affective states expressed in the items.

Thank you for this suggestion. However, all patients with bipolar disorder included in this study were required to fulfill strict euthymia criteria at the moment of the assessment. In addition, at the time of administering the TEMPS-A, all patients were specifically instructed to mark the "Yes" option only in those sentences that were applicable to them for most of their lives and to answer the questionnaire without taking into account those periods of time including acute episodes. From our point of view, we consider that, rather than being under pharmacological treatment, the presence of subsyndromal symptoms and other sociodemographic variables, such as gender and age, would be more responsible of potential temperamental profile differences between individuals and, for that reason, this was indeed considered as a limitation in the original submitted manuscript (see page 14, last paragraph).

9. The authors could also have applied other scales to better characterise external and discriminative validity of the instrument in this population. This, however, is rather an idea for further research. Also, hopefully the TEMPS-A data will be used for follow up in association with clinical course characteristics of bipolar disorder in the patient sample.

Thank you for these comments. We really agree with them. We are actually working on the design of different studies concerning TEMPS-A as a predictor of some clinical features associated with poor prognosis in bipolar disorder.

10. I was wondering if it is worth to enter the data in a regression model to see if temperaments predict bipolar was healthy grouping.

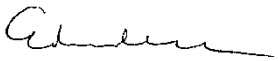
The present work’s main aim was to examine the psychometric properties of the Barcelona TEMPS-A with a special focus on its reliability and internal structure. Although we included a mixed sample consisting of patients with bipolar disorder and healthy controls, our goal was not to generate a predictive model. For this reason the study was neither designed nor powered to conduct this sort of statistical analyses. However, as suggested, we do not rule out the possibility to deeply explore the potential predictive role of the Barcelona TEMPS-A questionnaire along with other relevant clinical variables to distinguish between patients with bipolar disorder and healthy population in future studies.

Apart from the above suggestions and question the manuscript is well written, the applied methodology is sound, the results are well presented and the discussion is adequate give the data. The findings of the study are highly relevant from a clinical aspect.

Thank you very much for your comments.

We would like to express our gratitude to the reviewers for their effort and comments. We really hope that all the above described changes are going to fulfill your expectations and turn the paper into suitable for publication in your very prestigious journal. We thank you for the improvement in the final draft these changes have enhanced.

Yours sincerely,



Highlights:

- The Barcelona TEMPS-A presents a good internal consistency and inner structure and has been proved to be a reliable and valid tool to explore affective temperaments.
- This validation has been carried out with a large sample including patients with bipolar disorder and non-clinical population.
- The temperamental profile proved to remain stable over a wide period of time in euthymic patients with bipolar disorder.
- Psychometric properties of the Barcelona TEMPS-A are good, in line with the original scale and previous validations in other languages.

ABSTRACT

Background: The Temperament Evaluation of the Memphis, Pisa, Paris, and San Diego (TEMPS-A) is a self-administered questionnaire intended to assess five affective temperaments: depressive, cyclothymic, hyperthymic, irritable and anxious. Our objective was to examine the psychometric properties of the TEMPS-A using a sample comprised by patients with bipolar disorder (BD) and healthy controls (HC) and to determine cut-off scores for each temperament.

Methods: Five hundred and ninety-eight individuals (327 BD and 271 HC) completed the TEMPS-A. Cronbach's alpha was used to examine internal consistency reliability. Test-retest reliability and association between different temperamental scales were assessed using Spearman correlation. To confirm factor structure a confirmatory factor analysis (CFA) was carried out. Cut-off scores indicating the presence of dominant temperament were also calculated.

Results: Internal consistency was optimal for all temperament subscales (α: 0.682-0.893). The questionnaire demonstrated good test-retest reliability (ρ: 0.594- 0.754). The strongest positive associations were found between cyclothymic and anxious and between depressive and anxious temperaments. Hyperthymic and depressive as well as hyperthymic and anxious temperaments showed a strong negative correlation.

Limitations: The HC sample was not matched with the BD group. There were some sociodemographic and clinical differences between groups that may impact on the obtained results. A portion of patients with BD was recruited from tertiary centers.

Conclusions: The Spanish version of the Barcelona TEMPS-A questionnaire presents a good internal consistency and their results are stable in clinical population. The performance of the Barcelona TEMPS-A is as good as the original scale.

Spanish validation of the Barcelona TEMPS-A questionnaire in patients with bipolar disorder and general population

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Word count: 3.717

Number of figures: 0

Number of tables: 5

Spanish validation of the Barcelona TEMPS-A questionnaire in patients with bipolar disorder and general population

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Word count: 3.~~368~~717

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ABSTRACT

Background: The Temperament Evaluation of the Memphis, Pisa, Paris, and San Diego (TEMPS-A) is a self-administered questionnaire intended to assess five affective temperaments: depressive, cyclothymic, hyperthymic, irritable and anxious. Our objective was to examine the psychometric properties of the TEMPS-A using a sample comprised by patients with bipolar disorder (BD) and healthy controls (HC) and to determine cut-off scores for each temperament.

Methods: Five hundred and ninety-eight individuals (327 BD and 271 HC) completed the TEMPS-A. Cronbach's alpha was used to examine internal consistency reliability. Test-retest reliability and association between different temperamental scales were assessed using Spearman correlation. To confirm factor structure a confirmatory factor analysis (CFA) was carried out. Cut-off scores indicating the presence of dominant temperament were also calculated.

Results: Internal consistency was optimal for all temperament subscales (α: 0.682-0.893). The questionnaire demonstrated good test-retest reliability (ρ: 0.594- 0.754). The strongest positive associations were found between cyclothymic and anxious and between depressive and anxious temperaments. Hyperthymic and depressive as well as hyperthymic and anxious temperaments showed a strong negative correlation.

Limitations: The HC sample was not matched with the BD group. There were some sociodemographic and clinical differences between groups that may impact on the obtained results. A portion of patients with BD was recruited from tertiary centers.

Conclusions: The Spanish version of the Barcelona TEMPS-A questionnaire presents a good internal consistency and their results are stable in clinical population. The performance of ~~the Spanish version of~~ the Barcelona TEMPS-A is as good as the original scale.

Key words: TEMPS-A, validation, psychometric properties, Spanish, bipolar disorder, non-clinical population, temperament.

Highlights:

- The ~~analyzed version of the Spanish~~Barcelona TEMPS-A ~~questionnaire~~ presents a good internal consistency and inner structure and has been proved to be a reliable and valid tool to explore affective temperaments.
- This validation has been carried out with a large sample including patients with bipolar disorder and non-clinical population.
- The temperamental profile ~~obtained by means of the Barcelona TEMPS-A questionnaire~~ proved to remain stable over a wide period of time in euthymic patients with bipolar disorder.
- Psychometric properties of the Barcelona TEMPS-A ~~questionnaire~~ are good, in line with the original scale and previous validations in other languages.

INTRODUCTION

Based on Kretschmer's assumption of the existence of a continuum spectrum from the presence of extreme temperaments to full-blown affective illness, Akiskal and colleagues advocated the idea that affective temperaments play a substantial role in the predisposition to develop an affective disorder (Akiskal et al., 2005c;Akiskal et al., 2005d). The Temperament Evaluation of the Memphis, Pisa, Paris, and San Diego (TEMPS-A) was built on the base of the diagnostic criteria for affective temperaments. This questionnaire is divided into five subscales intended to examine discrete temperamental profiles: on one hand, depressive, cyclothymic, hyperthymic and irritable, which are clearly based on the Kraepelinian temperament proposal, and, on the other hand, the anxious temperament, based on a subscale drew up *a posteriori* by Hantouche and coworkers (Hantouche et al., 2005). This questionnaire differs from other scales based in other temperamental models more used to describe healthy personality, such as the Cloninger's model (Cloninger et al., 1993) and the Five Factor Model (Costa et al., 1985). In this sense, the TEMPS-A taps subaffective trait expression and frames questions in the language of affectivity (Akiskal et al., 2005b; Rozsa et al., 2008). Therefore, this instrument covers more specifically the temperamental assessment in people with affective disorders.

Several authors suggest that an accurate assessment of affective temperament may enhance to determine the potential risk of individuals to develop a major mood disorder such as major depression or bipolar disorder. Noteworthy, evidence suggest that specific temperaments have potential negative clinical implications in patients with bipolar disorder (BD), such as a worse prognosis (Perugi et al., 2012), a higher rate rate of comorbidity (Rybakowski et al., 2014) and suicidal behavior (Baldessarini et al., 2016;Jimenez et al., 2016;Rihmer et al., 2009;Tondo et al., 2018), a poorer drug response (de Aguiar et al., 2014;Rybakowski et al., 2013) and lower adherence (Solmi et al., 2016), amongst others. It is noteworthy that some specific affective temperaments have been also found to impact on smoking habits and on cardiovascular morbidity in psychiatrically healthy individuals (Eory et al., 2014;Eory et al., 2015;Nemcsik et al., 2017)

This self-administered questionnaire has been ~~widely~~ translated and validated in ~~across different countries in multiple~~ several languages, including Spanish (Sanchez-Moreno et al., 2007; Vazquez et al., 2007), American English (Akiskal et al., 2005b), French (Akiskal et al., 2005a), Portuguese (Figueira et al., 2008;Woodruff et al., 2011), Italian (Pompili et al., 2008), German (Bloink et al., 2005), Polish (Borkowska et al., 2010), Serbian (Ristic-Ignjatovic et al., 2014; Hinic et al., 2013), Hungarian (Rozsa et al., 2008), Greek (Fountoulakis et al., 2014), Turkish (Vahip et al., 2005) , Arabic (Karam et al., 2005), Mandarin (Lin et al., 2013), and Japanese (Matsumoto et al., 2005), becoming a key tool for measuring affective temperaments in the scientific community (Akiskal et al., 2005b,c;(Gonda et al., 2011);. It should be remarked that different short forms of this questionnaire are also available in different languages (Akiskal et al., 2005c; (Erfurth et al., 2005;Krebs et al., 2006;Nakato et al., 2016;Preti et al., 2010;Yuan et al., 2015).

This study aimed to study the psychometric properties of the Barcelona TEMPS-A, including the internal consistency and test-retest reliability, as well as to examine its factor structure in a non-clinical and clinical Spanish population consisting of patients with BD. A secondary purpose was to determine the prevalence of the Barcelona TEMPS-A dominant temperaments amongst Spanish population by means of preliminary cut-off scores for each temperament calculated on the one hand for the whole sample, and on the other for bipolar population and healthy controls, separately.

METHODS

Population

Seven-hundred and five volunteer participants from different regions of Spain were consecutively recruited and surveyed. Following the review and correction of the Barcelona TEMPS-A, all those questionnaires with any double answers or no-answers were discarded. Therefore, the final sample consisted of 598 individuals, out of which 327 were individuals diagnosed with BD, and 271 were healthy controls (HC).

Patients with BD were recruited from the Bipolar and Depression Disorder Unit of the Hospital Clinic of Barcelona, and mental health services from Oviedo, all under the umbrella of the Center of Biomedical Research Network on Mental Health (CIBERSAM) (Salagre et al., 2018). HC were recruited from both Barcelona and Granada via advertisement.

Inclusion criteria for all participants were: a) being aged 18 or older and b) providing a written informed consent. In the case of bipolar patients they should also i) present a diagnosis of bipolar disorder following DSM-IV-TR criteria, ii) fulfill strict euthymia criteria at the moment of the assessment (Hamilton Depression Rating Scale (HDRS)≤8 (Hamilton, 1960;Ramos-Brieva et al., 1986) and Young Mania Rating Scale (YMRS)≤6 (Colom et al., 2002;Young et al., 1978). Exclusion criteria for all the participants were: i) history of mental retardation or ii) any medical condition that could interfere in the assessment procedure. ~~Additionally, a history of mental illness and previous or current use of prescribed psychotropic drugs were considered as exclusion criteria for the healthy control participants.~~ All healthy volunteers were also screened for personal and family history of any psychiatric condition. Therefore, a history of mental illness and previous or current use of prescribed psychotropic drugs were considered as exclusion criteria for the healthy control participants. Additionally, all those healthy controls reporting to have a first-degree relative with any psychiatric condition were also excluded from the study. All patients who agreed to a second administration of the TEMPS-A later in time also had to meet baseline inclusion and exclusion criteria. Approval from each institution's ethics committees was obtained.

Measures

Affective temperaments were assessed by means of the Barcelona TEMPS-A questionnaire. This self-applied instrument consists of 110 items (109 in the case of males) which requires a "true/false" response and assesses the presence of five affective temperaments, namely: depressive (items 1-21), cyclothymic (items 22-42), hyperthymic (items 43-63), irritable (items 64-84) and anxious (items 85-110). Each

subscale comprises 21 items, except the anxious one which has 26 in the Spanish examined version. All the Barcelona TEMPS-A items were scored "Yes" as 1 and "No" as 0. This instrument has two available Spanish versions, one from Buenos Aires which has been previously validated in a non-clinical population (Vazquez et al., 2007), and another one translated and adapted by our group in Barcelona (Sanchez-Moreno et al., 2005), which is the one which was used in the current study.

Sociodemographic data (gender, age, and years of education) were gathered from all participants. Concerning patients with BD, diagnosis was confirmed by experienced mental health professionals and following DSM-IV-TR criteria. The remaining clinical data were collected during a semi-structured interview based on the SCID and verified by a medical record review. The presence of depressive and manic symptomatology was assessed using the HDRS and the YMRS, respectively, in the total sample. The same procedure was replicated in those patients with BD who agreed to a second administration of the Barcelona TEMPS-A later in time.

Statistical Analysis

Firstly, normality of data was tested using the Kolmogorov-Smirnov test and by analyzing the Q-Q plots and data distribution in the histograms. Levene's test was used to evaluate homogeneity of variance. Noteworthy, none of the explored variables were normally distributed, even when total sample was divided according to clinical status (BD vs HC).

Descriptive statistics (means, standard deviations, median, and 95th percentile) were calculated for both the entire questionnaire and each subscale. Differences in sociodemographic and clinical data between patients with BD and HC were computed with non-parametric U Mann-Whitney test and Chi squared, as appropriate. Differences among clinical and HC groups concerning the presence of dominant temperament (scores ≥95th percentile) were explored using Chi-square test or Fisher's exact test, as convenient. Spearman correlation was carried out in order to determine the presence or absence of correlations and also to explore test-retest reliability and consistency.

The internal consistency of the temperamental domains was either measured by Cronbach's alpha. Despite there is no clear cut-off, there is consensus considering that scores above 0.7 indicate an optimal internal consistency (Taber, 2017).

A Confirmatory Factor Analysis (CFA) was carried out in order to confirm factor structure of the Barcelona TEMPS-A. Bearing in mind that original TEMPS-A version comprises five factors, we forced the extraction of five main components using Varimax rotation. For this purpose, we used some fit indexes: the root mean square error of approximation (RMSEA), with values ≤0.05 indicating good fit and ≤0.01, excellent fit (MacCallum et al., 1996); the standardized root mean square residual (SRMR), scores ≤0.09 are considered acceptable; the Tucker Lewis index or Non-normed Fit Index (TLI): the higher scores, the better. Values >0.9 are indicative of good fit (Hu L. et al., 1999); and, finally, the Schwarz's Bayesian information criterion (BIC), which is considered as a more conservative index with which lower scores are desirable (Schwarz, 1978). CFA analysis was conducted with the psych package (Revelle, 2018) running in R (R Development Core Team, 2008). The aforementioned package includes different functions mostly used for psychometric research.

All data was analyzed using SPSS v.23 with the exception of the CFA which was carried out by means of R, as mentioned above. Significance level was set at $p<0.05$.

RESULTS

Sociodemographic and clinical data

The final sample consisted of 598 participants including 327 patients with BD and 271 HC. Participants were aged from 18 to 81 (mean=40.83; SD=12.505) years. HC were younger in average (BD=44.61 vs HC=36.27; Mann-Whitney U=60.882; $p<0.001$), presented higher rates of female participants (BD=48.3% vs HC=65.3%; χ^2= 17.374; $p<0.001$), had less subthreshold depressive symptoms (HDRS: BD=3.79 vs HC=1.87; Mann-Whitney U=15.201; $p<0.001$), but no differences were detected within the groups concerning the presence of subsyndromal manic symptoms (YMRS: BD=1.25 vs

HC=0.69; Mann-Whitney U=9.844; p=0.130).

Reliability

Internal consistency of the temperament subscales together with main descriptive statistics are displayed in Table 1. Cronbach's alpha values were obtained from the whole sample as well as from BD and HC subsamples. Results indicated that all domains of the examined version of the Barcelona TEMPS-A present an adequate internal reliability, ranging from 0.682 to 0.893, being the depressive subscale which showed the lowest values, and the cyclothymic subscale which presented the strongest one. Of note, the item analysis revealed that item 14 discriminates negatively with the depressive subscale and its extraction would imply an increase in reliability value (from 0.682 to 0.691) in the non-clinical subsample only.

Differences between HC and BD concerning Barcelona TEMPS-A scores

Patients with BD scored on average significantly higher in the depressive (BD=9.66 vs HC=7.65; Mann-Whitney U=56.646; p<0.001), the cyclothymic (BD=8.33 vs HC=5.14; Mann-Whitney U=58.934; p<0.001), the irritable (BD=4.47 vs HC=3.76; Mann-Whitney U=48.772; p=0.033) and the anxious temperament (BD=9.72 vs HC=7.31; Mann-Whitney U=54.292; p<0.001).- However, HC scored significantly higher than patients with BD in the hyperthymic temperament (BD=7.97 vs HC=10.25; Mann-Whitney U=31.452; p<0.001).

Differences between HC and BD concerning rates of dominant temperaments

Since none of the scores was found to be normally distributed, we calculated the 95th percentile of raw scores in order to determine the presence or absence of dominant temperaments. Therefore, individuals scoring equal or above the aforementioned percentile were classified as presenting a dominant temperament. Three different cut-offs were calculated for each temperament subscale: for the whole sample, for the BD and the HC subsamples (see Table 1).). According to each subsample cut-off scores (BP and HC, respectively), no differences between rates of dominant temperament between groups were observed (See Table 2). However, when participants were

classified according to the whole sample cut-off, increased percentages of dominant temperament were found in the BD group in the depressive (BD=10.7% vs HC=1.1%; χ^2=22.933; p<0.001), the cyclothymic (BD=10.1% vs HC=1.5%; χ^2=18.961; p<0.001), and the anxious temperament (BD=8.9% vs HC=3.7%; χ^2= 6.518; p<0.012) (see Table 3). No differences were observed concerning the remaining temperaments between clinical and non-clinical population.

Considering each subsample cut-off scores, the rates of dominant temperaments observed in the subsample of patients with BD were as follows: hyperthymic (8.3%), depressive (7.3 %), anxious (6.1 %), cyclothymic and irritable temperament (both 5.5%), respectively. In change, in the HC group, the higher rate of dominant temperament was observed in the irritable temperament (7.0%) followed by the cyclothymic, hyperthymic (both 5.5%), depressive and anxious temperaments (5.2%, each). Nonetheless, no statistical significant differences between groups were found when each subsample cut-off was used (see Table 2).

Correlations between temperament subscales

Correlations among the five temperament subscales are reported in Table 4. Despite most of the temperament subscales were highly associated, the strongest positive associations were detected between cyclothymic and anxious temperaments (whole sample: ρ= 0.710; BD: ρ=0.720; HC: ρ=0.664) as well as depressive and anxious (whole sample: ρ= 0.693; BD: ρ=0.704; HC: ρ =0.652). On the other hand, the largest negative correlation was observed between hyperthymic and depressive subscales (whole sample: ρ=-0.327; BD: ρ=-0.322; HC: ρ=-0.235) and hyperthymic and anxious temperaments (whole sample: ρ= -0.197; BD: ρ=-0.161; HC: ρ=-0. 155). No associations were found between hyperthymic and irritable temperaments or between hyperthymic and cyclothymic subscales.

Test-retest stability

Of the 327 bipolar participants, a subset of 65 agreed to reassessment later in time.

The retest temporal interval ranged from 3 months to 8 years and 6 months (mean=38.54 months). Test-retest correlation was 0.754 for the depressive , 0.693 for the cyclothymic, 0.683 for the hyperthymic, 0.594 for the irritable and 0.748 for the anxious temperament, indicating an adequate retest reliability of the Barcelona TEMPS-A among patients with BD over time.

Confirmatory Factor Analysis

A principal component analysis was carried out to confirm the *a priori* expected five-factor model of the examined version of the TEMPS-A scale. The obtained model exhibited an optimal model fit (RMSEA: 0.036; RMSR: 0.04; TLI: 0.774; BIC: -25891.25) and accounted for 26% of the total variance (see factor loadings in Table 5).

The first component, which accounted for the 10% of the total variance, consisted of a mixture of different traits. All the items comprised in the original cyclothymic subscale except one were included in this first component, as well as a mixture of anxious and depressive and few irritable traits. The second factor was mainly consisting of irritable items, and few items concerning somatic anxious symptoms. The third component represents mostly hyperthymic traits with two items from the original depressive subscale with negative loading on the factor. The fourth involves a blend of irritable and anxious traits. And finally, the fifth component was mostly composed of anxious and depressive features.

DISCUSSION

The main goal of this study was to examine the internal structure, reliability and stability of the Barcelona TEMPS-A questionnaire using a large sample of patients with BD and non-clinical individuals. Results from our study indicate that this Spanish version TEMPS-A questionnaire has good internal consistency ranging from alpha values in the whole sample of 0.766 to 0.890. Of note, the depressive subscale showed a slightly lower Cronbach's alpha score (0.682) in the HC subsample. This result was also found in prior studies that also reported a slightly lower internal consistency of

the depressive subscale in non-clinical population (Bloink et al., 2005;Dolenc et al., 2013;Karam et al., 2005;Lin et al., 2013;Matsumoto et al., 2005).

With regards to affective temperament scores, the BD group presented higher scores when compared to the HC group in all subdomains except for the hyperthymic temperament, whose scores resulted higher in the HC group. Higher scores of temperament subtypes in BD have also been described in a recent meta-analysis by Solmi et al. (2016), who compared in twenty-six studies TEMPS-A scores between different clinical and non-clinical groups. We also aimed to ascertain rates of dominant temperaments based on preliminary cut-off scores for each temperament. Using the whole sample cut-off scores, we observed significant differences between groups, the cyclothymic, depressive and anxious temperaments being the most prevalent in the BD group. From a clinical perspective, the high co-occurrence of the anxious temperament along with cyclothymic and depressive temperaments among the BD group is far from being unexpected due to the high prevalence of comorbid anxiety disorders in BD (Pavlova et al., 2015;Vazquez et al., 2014) and due to the presence of anxious symptomatology during acute episodes independently of their polarity. The higher rates of cyclothymic dominant temperament among patients with BD were not surprising either, since cyclothymia has been also widely associated with the emergence of this psychiatric condition. Of note, cyclothymia describes everything from temperament to a prodrome of BD and it has been estimated that more than one third of patients diagnosed as cyclothymic would develop BD, mainly BD type II (Vieta et al., 2018). On the contrary, the high prevalence of the hyperthymic temperament in HC surprises as several prior works reported very low rates of the hyperthymic dominant temperament across non clinical population (Vazquez et al., 2007; Fountoulakis et al., 2014; Karam et al., 2005; Lin et al., 2013; (Placidi et al., 1998). We hypothesize that this result in our sample might be considered as a differential *"illness awareness"* between both groups of participants. It is possible that patients with BD are more aware of the negative impact of hyperthymic features and they may easily identify them as more pathological, influencing the way they respond to items assessing this temperament and resulting in a negative response bias. In contrast, HC may consider some hyperthymic items as socially acceptable and probably as

indicators of good mood. However, it should be mentioned that Rozsa and colleagues reported that rates of dominant hyperthymic temperament were mainly as high as depressive in a large sample of healthy volunteers. Moreover, when rates between genders were compared, the hyperthymic was one of the most prevalent dominant temperaments among men, only surpassed by cyclothymic temperament (Rosza et al., 2008).

In general lines, our results indicate that the five temperaments are not independent from each other, replicating results obtained by several prior works (Borkowska et al., 2010;Dolenc, Sprah, Dernovsek, Akiskal, and Akiskal, 2013;Fountoulakis et al., 2014;Lin, Xu, Miao, Ning, Ouyang, Chen, Hoang, Akiskal, and Akiskal, 2013;Vazquez et al., 2007). In our whole sample, as well as in each subsamples (BD and HC), the largest correlations were observed between the cyclothymic and the anxious, the anxious and the depressive, and the cyclothymic and the irritable temperament. As a matter of fact, Fountoulakis and colleagues (2014) suggested that the association between anxious, cyclothymic and depressive temperaments resembles to Eysenck's neuroticism personality trait and remarked the role of these associations, especially between cyclothymic and anxious temperaments as a potential substrate of bipolar II disorder diagnosis (Fountoulakis et al., 2014). As stated before, the association between these three dimensions was not surprising as the lifetime prevalence of any anxiety disorder in BD has been estimated to be around 45% (Pavlova et al., 2015).

In line with several prior works, our results also point towards a presence of negative correlations between hyperthymic and depressive temperaments. These results comport with previous studies and are in compliance with the so-called "biphasic spectrum" hypothesis (Vazquez et al., 2007; Dolenc et al., 2013; Fountoulakis et al., 2014; Bloink et al., 2005), which claims that those affective traits are distributed across population with depressive features in one pole and hyperthymic traits in the opposite side and they are, at least in some extent, mutually exclusive.

Despite literature is teeming with results indicating that temperamental profile obtained by means of the TEMPS-A remain stable throughout time in non-clinical population (Akiskal et al., 2005b;Elias et al., 2017;Hinic et al., 2013;Kawamura et al.,

2010;Lin, Xu, Miao, Ning, Ouyang, Chen, Hoang, Akiskal, and Akiskal, 2013;Matsumoto, Akiyama, Tsuda, Miyake, Kawamura, Noda, Akiskal, and Akiskal, 2005;Ristic-Ignjatovic et al., 2014;Vahip et al., 2005), few studies have explored test-retest stability in clinical samples so far. In our study the test-retest reliability analysis confirms that results obtained from the examined version of the TEMPS-A remains stable over a wide range of time (ranging from 3 to 102 months) with correlations ranging from 0.683 to 0.754. Therefore our results suggest that stability of the Barcelona TEMPS-A temperamental profile is also guaranteed in BD beyond time, at least when patients are evaluated during euthymia.

The goodness-of-fit levels of our version of the TEMPS-A proved to be optimal in terms of all the obtained indices. Additionally, and in line with previous works, CFA results confirm the a priori expected five-factor structure of the TEMPS-A and it also remarks the solidity of the hyperthymic temperament, since it can be considered rather distinct from the depressive, cyclothymic, irritable and anxious temperaments. Moreover, items composing this subscale tend to cluster together in contrast with what happens to items belonging to the rest of items from other temperament subscales of the original version (Vazquez et al., 2007; Dolenc et al, 2017). On the contrary, based on our CFA results, the anxious temperament appears as a blurred domain, since its items are scattered amongst the different temperamental subdomains. In this sense and partially in line with our results, it should be remarked that the solidity of this scale has been also questioned by other authors, such as Woodruff and colleagues (2011) who proposed to split this domain into two factors: physical symptoms and worrying items (Woodruff et al., 2011). This has been also supported by Ristic-Ignjatovic and collaborators (2014) who found evidence for the division of the anxiety scale into two different subscales, namely, cognitive and somatic anxiety. Nonetheless, and according to other authors, we are in favor of the idea that differential item assignment concerning temperamental subscales may be influenced by cultural differences (Fountoulakis et al., 2014) and in keeping the TEMPS-A original structure.

There are some limitations to be considered. Firstly, even though we included a mixed sample of clinical and non-clinical individuals, which is a methodological strength of this study, both groups were not matched. Differences concerning age, gender and

subsyndromal ~~depressive~~ features, even during euthymia, do not allow us to rule out the fact that differences concerning temperamental patterns prevalence may be influenced by differences in the aforementioned variables between both groups. Another limitation relates to the absence of other validated instruments as comparators in order to assess convergent validity. Finally, it should be mentioned that a substantial part of patients with BD were recruited from a tertiary center. Thus, some participants could be categorized as difficult-to-treat patients and generalizability of results may be somewhat restricted (Vieta, 2011).

In conclusion, the psychometric properties of the Barcelona TEMPS-A questionnaire has shown to be optimal indicating that it is a reliable, valid and stable tool for the assessment of temperament profile in both non-clinical populations and patients with BD. Further validation studies with mixed samples of non-clinical and different psychiatric populations are needed in order to determine its usefulness in the assessment of other mental conditions.

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	Temperament	Depressive (max: 21)	Cyclothymic (max: 21)	Hyperthymic (max: 21)	Irritable (max: 21)	Anxious (max: 25)
Total Sample	**Cronbach's alpha**	0.766	0.890	0.811	0.815	0.874
	Mean	8.75	6.88	9.00	4.15	8.63
	SD	3.924	5.383	4.595	3.724	5.827
	Median	8	6	9	3	8
	95th percentile	16	17	16	12	19
Bipolar disorder	**Cronbach's alpha**	0.778	0.893	0.823	0.812	0.882
	Mean	9.66	8.33	7.97	4.47	9.72
	SD	4.240	5.638	4.658	3.893	6.077
	Median	9	8	8	4	9
	95th percentile	17	18	16	13	20
Healthy controls	**Cronbach's alpha**	0.682	0.858	0.765	0.817	0.850
	Mean	7.65	5.14	10.25	3.76	7.31
	SD	3,181	4.483	4.199	3.476	5.226
	Median	7	4	10	3	7
	95th percentile	14	15	17	10	18

Abbreviations: SD= standard deviation

Table 1: Reliability analysis results and descriptive statistics of the total sample, the BD and HC groups.

Temperament	Depressive		Cyclothymic		Hyperthymic		Irritable		Anxious	
	BD	***HC***	***BD***	***HC***	***BD***	***HC***	***BD***	***HC***	***BD***	***HC***
Cut-off	17	14	18	15	16	17	13	10	20	18
N	24	14	18	15	27	15	18	19	20	14
%	7.3	5.2	5.5	5.5	8.3	5.5	5.5	7	6.1	5.2

Abbreviations: BD= Bipolar disorder group; HC= Healthy control group.

Table 2: Frequencies and percentages of dominant temperament according to two different cut-off scores for bipolar patients and healthy controls.

Temperament	*BD*	*HC*	*Chi-square*	*p-value*
Depressive Cut-off=16	35 (10.7%)	3 (1.1%)	22.933	**<0.001***
Cyclothymic Cut-off=17	33 (10.1%)	4 (1.5%)	18.961	**<0.001***
Hyperthymic Cut-off=16	27 (8.3%)	33 (12.2%)	2.523	0.133
Irritable Cut-off=12	21 (6.4%)	11 (4.1%)	1.634	0.273
Anxious Cut-off=19	29 (8.9%)	10 (3.7%)	6.518	**0.012**

*Fisher exact Test

Abbreviations: Bipolar disorder group; HC= Healthy control group.

Table 3: Frequencies and percentages of dominant temperament according to whole sample cut-off scores.

Whole sample temperament	**Depressive**	**Cyclothymic**	**Hyperthymic**	**Irritable**
Depressive				
Cyclothymic	**.620****			
Hyperthymic	**-.327****	-.056		
Irritable	**.449****	**.640****	.070	
Anxious	**.693****	**.710****	**-.197****	**.611****

BD temperament	**Depressive**	**Cyclothymic**	**Hyperthymic**	**Irritable**
Depressive				
Cyclothymic	**.591****			
Hyperthymic	**-.322****	-.013		
Irritable	**.460****	**.668****	.101	
Anxious	**.704****	**.720****	**-.161****	**.636****

HC temperament	**Depressive**	**Cyclothymic**	**Hyperthymic**	**Irritable**
Depressive				
Cyclothymic	**.584****			
Hyperthymic	**-.235****	.060		
Irritable	**.429****	**.602****	.080	
Anxious	**.652****	**.664****	**-.155***	**.570****

**p<0.001; * p<0.05

Abbreviations: Bipolar disorder group; HC= Healthy control group.

Table 4: Spearman's correlations between the TEMPS-A subscales concerning whole sample, and bipolar and healthy control subsamples.

Item		COMPONENT				
		1	4	2	5	3
Cyc_29	**Mi estado de ánimo cambia a menudo sin ningún motivo** *(My mood often changes for no reason)*	**0.69**				
Cyc_25	**Mi habilidad para pensar varía mucho, pasando de ser aguda a torpe sin ningún motivo aparente** *(My ability to think varies greatly from sharp to dull for no apparent reason)*	**0.64**				
Cyc_38	**La manera en que veo las cosas es a veces intensa, pero otras veces apagada (anodina)** *(The way I see things is sometimes vivid, but at other time lifeless)*	**0.63**				
Cyc_30	**Paso constantemente de ser vital a ser inactivo** *(I constantly switch between being lively and sluggish)*	**0.63**				
Cyc_23	**Tengo cambios repentinos de humor y energía** *(I get sudden shifts in mood and energy)*	**0.62**				
Cyc_24	**Mi ánimo y energía son altos o bajos, raramente normales** *(My moods and energy are either high or low, rarely in between)*	**0.62**				
Cyc_34	**Paso de tener mucha confianza en mí mismo a sentirme inseguro** *(I go back and forth between being overconfident and feeling unsure of myself)*	**0.59**				
Cyc_22	**A menudo me siento cansado sin motivo** *(I often feel tired with no reason)*	**0.56**				
Cyc_35	**Paso de ser abierto a ser retraído con los demás** *(I go back and forth between being outgoing and being withdrawn from others)*	**0.54**				
Anx_92	**A menudo me siento muy inquieto por dentro** *(I often feel jittery inside)*	**0.53**				
Cyc_28	**A menudo empiezo cosas perdiendo el interés antes de acabarlas** *(I often start things and the lose interest before finishing them)*	**0.52**				
Irr_70	**Me siento impulsado por una inquietud desagradable que no comprendo** *(I am driven by an unpleasant restlessness that i do not understand)*	**0.51**				
Cyc_33	**Me dicen que a menudo me pongo pesimista y que olvido los tiempos felices del pasado** *(I am told that often get pessimistic about things and forget previous happy times)*	**0.50**				

		1	4	2	5	3
Cyc_32	**A veces me voy a la cama sintiéndome fenomenal y me levanto por la mañana sintiendo que no vale la pena vivir** *(I sometimes go to bed feeling great , and wake up in the morning feeling life is not worth living)*	**0.50**				
Cyc_37	**Mi necesidad de dormir cambia mucho, pasando de necesitar unas pocas horas de sueño a más de 9 horas** *(My need for sleep varies a lot from just a few hours to more than 9 hours)*	**0.47**				
Cyc_26	**Puedo pasar de que alguien me guste mucho a perder totalmente el interés en esa persona** *(I can really like someone a lot, and then completely lose my interest in them)*	**0.46**				
Anx_86	**Me preocupo siempre por una cosa u otra** *(I am always worrying about one thing or another)*	**0.46**				
Dep_5	**Abandono fácilmente** *(I give up easily)*	**0.45**				
Anx_87	**Me siguen preocupando cosas cotidianas que los demás consideran poco importantes** *(I keep on worrying about daily matters that others consider minor)*	**0.45**				
Anx_108	**Incluso pequeños cambios en la rutina me estresan mucho** *(Even minor changes in routine stress me highly)*	**0.44**				
Dep_7	**Siempre me he sentido culpable por cosas que los demás considerarían poco importantes** *(I have always blamed myself for what others might consider no big deal)*	**0.43**				
Anx_88	**No puedo hacer nada para dejar de preocuparme** *(I cannot help worrying)*	**0.43**				
Anx_89	**Mucha gente me ha dicho que no me preocupe tanto** *(Many people have told me not to worry so much)*	**0.42**				
Irr_69	**A menudo me siento muy nervioso** *(I often feel wound up)*	**0.41**				
Anx_107	**Soy una persona insegura** *(I am an insecure person)*	**0.41**				
Dep_1	**Soy una persona triste, infeliz** *(I am a sad, unhappy person)*	**0.41**				
Dep_3	**He sufrido mucho en la vida** *(I have suffered a lot in life)*	**0.40**				
Anx_90	**Cuando estoy estresado, a menudo mi mente se queda en blanco** *(When stressed, my mind often goes blanck)*	**0.40**				
Cyc_39	**Soy el tipo de persona que puede estar triste y contenta a la vez** *(I am the kind of person who can be sad and happy at the same time)*	**0.40**				

		1	4	2	5	3
Irr_68	**A menudo me siento en el límite** *(I often feel on edge)*	**0.38**				
Dep_4	**Pienso que a menudo las cosas salen mal/peor** *(I think things often turn out for the worst)*	**0.37**				
Anx_93	**Cuando estoy estresado, a menudo me tiemblan las manos** *(When stress, my hands often tremble)*	**0.36**				
Dep_8	**No tengo tanta energia como otras personas** (I do not seem to have as much energy as other people)	**0.35**				
Dep_13	**Me siento fácilmente herido por las críticas y el rechazo** *(My feelings are easily hurt by criticism or rejection)*	**0.35**				
Anx_91	**Soy incapaz de relajarme** *(I am unable to relax)*	**0.34**				
Dep_19	**Soy el tipo de persona que duda de todo** *(I am the kind of person who doubt everything)*	**0.33**				
Cyc_40	**Muy a menudo sueño despierto cosas que otras personas consideran imposibles de conseguir** *(I daydream a great deal about things that other people consider impossible to achieve)*	**0.31**				
Dep_6	**Desde siempre me he sentido un fracasado** *(As long as I can remember, I have felt like a failure)*	**0.30**				
Cyc_41	**A menudo tengo un fuerte impulso de hacer cosas escandalosas** (I often have a strong urge to do outrageous things)	**0.30**				
Anx_101	**Mi sueño no es descansado** *(My sleep is not restful)*	**0.30**				
Cyc_36	**Siento todas las emociones intensamente** *(I feel my emotions intensily)*	**0.30**				
Dep_21	**Normalmente necesito dormir más de 9 horas** *(I normally need more than 9 hours of sleep)*	**0.30**				
Cyc_31	**A veces me voy a la cama triste pero me levanto por la mañana sintiéndome fantástico** *(I sometimes go to bed feeling down and wake up in the morning feeling terrific)*	**0.30**				
Anx_102	**Frecuentemente tengo dificultad para dormirme** (I frequently have difficulty falling asleep)	**0.29**				
Anx_85	**Que yo recuerde siempre he sido una persona aprensiva** *(I have been a worrier for as long as I can remember)*	**0.29**				

		1	4	2	5	3
Cyc_42	**Soy el tipo de persona que se enamora y desenamora fácilmente** *(I am the kind of person who falls in and out in love easily)*	**0.28**				
Dep_20	**Mi deseo sexual ha sido siempre bajo** *(My sex drive has always been low)*	**0.23**				
Anx_94	**A menudo tengo molestias en el estómago** *(I often have an upset stomach)*	**0.22**				
Irr_67	**Soy muy crítico con los demás** *(I am highly critical of others)*		**0.53**			
Irr_66	**Me quejo mucho** *(I complaint a lot)*		**0.49**			
Irr_73	**La gente me dice que exploto por nada** *(People tell me I blow up out of nowhere)*		**0.46**			
Irr_64	**Soy una persona malhumorada (Irritable)** (I am a grouchy (Irritable) person)		**0.45**			
Irr_65	**Soy una persona insatisfecha por naturaleza** *(I am by nature a dissatisfied person)*		**0.43**			
Cyc_27	**A menudo exploto con la gente y luego me siento culpable** *(I often blow up at people and then feel guilty about it)*		**0.41**			
Irr_77	**Puedo ponerme tan furioso que puedo herir a alguien** *(I can get so furious I could hurt someone)*		**0.40**			
Hyp_61	**Cuando no estoy de acuerdo con alguien puedo meterme en una discusión acalorada** *(When I disagree with someone, I can get into a heated argument)*		**0.37**			
Dep_2	**La gente dice que soy incapaz de ver el lado bueno de las coses** *(People tell me I am unable to see the lighter side of things)*		**0.37**			
Irr_81	**Soy una persona muy escéptica** *(I am a very skeptical person)*		**0.33**			
Irr_74	**Cuando me enfado, contesto mal** *(When angry, I snap at people)*		**0.31**			
Anx_96	**Cuando estoy nervioso a menudo tengo náuseas** (When I am nervous, I often feel nauseous)		**0.29**			
Irr_76	**Mi humor corrosivo me ha metido en problemas** *(My biting humour has gotten me into trouble)*		**0.29**			

		1	4	2	5	3
Irr_82	**Podría ser un revolucionario** *(I could be a revolutionary)*		**0.28**			
Hyp_56	**La gente me dice que a menudo meto la nariz en los asuntos de los demás** *(People tell me I often get my nose into other business)*		**0.24**			
Anx_97	**Cuando estoy nervioso tengo que ir con frecuencia al baño** *(When I am nervous, I have to go to the bathroom more often)*		**0.23**			
Anx_95	**Cuando estoy nervioso puedo tener diarrea** *(When I am nervous, I may have diarrhea)*		**0.20**			
Hyp_51	**Tengo un don para el habla, convenzo e inspiro a los demás** *(I have a gift for speech, convincing and inspiring others)*			**0.57**		
Hyp_48	**A menudo tengo grandes ideas** *(I often get many great ideas)*			**0.55**		
Hyp_47	**Tengo gran confianza en mí mismo** *(I have great confidence in myself)*			**0.53**		
Hyp_52	**Me gusta emprender nuevos proyectos, aunque sean arriesgados** *(I love to tackle new projects, even if risky)*			**0.53**		
Hyp_54	**Me siento totalmente cómodo, incluso estando con personas que apenas conozco** *(I am totally comfortable even with people I hardly know)*			**0.52**		
Hyp_50	**Puedo hacer muchas cosas sin cansarme** *(I can accomplish many tasks without even getting tired)*			**0.50**		
Hyp_55	**Me encanta estar con mucha gente** *(I love to be with a lot of people)*			**0.49**		
Hyp_43	**Mi estado de ánimo es generalmente optimista y alegre** *(I am usually in an upbeat or cheerful mood)*			**0.47**		
Hyp_45	**Me gusta contar chistes, la gente me dice que soy muy divertido** *(I like telling jokes, people tell me I am humorous)*			**0.45**		
Hyp_49	**Estoy siempre de acá para allá** *(I am always on the go)*			**0.45**		
Hyp_44	**La vida es una fiesta que disfruto al máximo** *(Life is a feast which I enjoy to the fullest)*			**0.43**		
Hyp_46	**Soy el tipo de persona que cree que finalmente todo saldrá bien** *(I am the kind of person who believes everything will eventually turn out all right)*			**0.39**		

		1	4	2	5	3
Hyp_53	**Una vez decido hacer algo nada puede detenerme** *(Once I decide to accomplish something, nothing can stop me)*			**0.34**		
Dep_12	**Me siento muy inseguro al conocer a gente nueva** *(I feel very uneasy meeting new people)*			**-0.34**		
Hyp_57	**La gente me considera una persona generosa, que gasta mucho dinero en los demás** (I am generous, and spend a lot of money on other people)			**0.31**		
Hyp_62	**Mi deseo sexual es siempre alto** *(My sex drive is always high)*			**0.30**		
Hyp_63	**Normalmente puedo pasar con menos de 6 horas de sueño** *(Normally I can get by with less than 6 hours of sleep)*			**0.30**		
Hyp_59	**Siento que tengo el derecho y el privilegio de hacer lo que yo quiera** *(I feel I have the right and privilege to do as I please)*			**0.29**		
Hyp_58	**Tengo habilidades y conocimientos en muchas áreas** *(I have abilities and expertise in many areas)*			**0.27**		
Irr_75	**Me gusta tomar el pelo a la gente, incluso a la que apenas conozco** *(I like to tease people, even those I hardly know)*			**0.26**		
Dep_9	**Soy la clase de persona a la que no le gustan demasiado los cambios** *(I am the kind of person who does not like change very much)*			**-0.25**		
Anx_100	**Siempre estoy pensando que alguien pueda darme malas noticias sobre un miembro de mi familia** *(I am always thinking someone might break bad news to me about a family member)*				**0.47**	
Anx_104	**A menudo me despierto por la noche asustado pensando si hay ladrones en casa** *(I often woke up at night afraid that burglars are in the house)*				**0.43**	
Irr_83	**Mi deseo sexual es a menudo tan intenso que llega a ser realmente desagradable** *(My sex drive is often so intense that it is truly unpleasant)*				**0.42**	
Irr_72	**Cuando estoy de mal humor podría enzarzarme en una pelea** *(When crossed, I could get into a fight)*				**0.41**	
Anx_99	**A menudo temo que alguien de mi familia contraiga una enfermedad grave** *(I am often fearful of someone in my family coming down with a serious disease)*				**0.41**	
Irr_71	**A menudo me enfado tanto que lo destrozaría todo** *(I often get so mad that I will just trash everything)*				**0.37**	
Irr_84	**(Mujeres solo): Tengo ataques incontrolables de ira antes de la menstruación** *(Women only: I have attacks of uncontrollable rage right before my periods)*				**0.34**	

		1	4	2	5	3
Irr_80	**Me han dicho que me pongo violento con solo unas copas** *(I have been told that I become violent with just a few drinks)*				**0.30**	
Irr_78	**Soy tan celoso de mi pareja que no puedo soportarlo** *(I am so jealous of my spouse (or lover), that cannot stand it)*				**0.29**	
Anx_109	**Cuando conduzco, incluso aunque no he hecho nada incorrecto, tengo miedo de que la policía pueda pararme** *(While driving even when I have not done anything I fear that police may stop me)*				**0.28**	
Irr_79	**La gente dice que digo muchos tacos** *(I am known to swear a lot)*				**0.25**	
Dep_16	**Soy una persona muy trabajadora** *(I am a hard working person)*					**0.36**
Dep_15	**Pongo las necesidades de los demás por encima de las mías** *(I put the needs of others above my own)*					**0.35**
Anx_103	**Soy, por naturaleza, una persona muy cautelosa** ***(****I am by nature a very cautious person)*					**0.33**
Anx_98	**Cuando alguien tarda en volver a casa temo que haya tenido un accidente** *(When someone is late coming home, I fear they may have had an accident)*					**0.32**
Dep_11	**A menudo cedo ante los demás** *(I often give in to others)*					**0.31**
Hyp_60	**Soy el tipo de persona a la que le gusta ser el jefe** *(I am the kind of person who likes to be the boss)*					**-0.31**
Dep_14	**Soy el tipo de persona con la que siempre se puede contar** *(I am the kind of person you can always depend on)*					**0.30**
Dep_17	**Preferiría trabajar para otra persona que ser el jefe** *(I would rather work for someone else than be the boss)*					**0,29**
Anx_106	**Cuando estoy estresado siento una sensación desagradable en el pecho** *(When stressed, I get an uncomfortable feeling in my chest)*					**0.28**
Dep_18	**Es natural en mí ser pulcro y organizado** *(It is natural for me to be neat and organized)*					**0.28**
Dep_10	**Cuando estoy en grupo prefiero escuchar a los demás** *(In a group, I would rather hear others talk)*					**0.28**
Anx_110	**Los ruidos inesperados me sobresaltan fácilmente** *(Sudden noises startle me easily)*					**0.27**

		1	**4**	**2**	**5**	**3**
Anx_105	**Cuando estoy estresado fácilmente sufro dolores de cabeza** *(I easily get headaches when stressed)*					**0.22**

Italics indicate the original English items, which have been added to enhance readers' understanding.
Dep: Depressive item; Cyc: Cyclothymic item; Hyp: Hyperthymic item; Irr: Irritable item; Anx: Anxious item.

Table 5: Component structure of the Barcelona TEMPS-A questionnaire after Varimax rotation.

Conflict of Interests

Dr. Benabarre has received research grants and served as a speaker for the following companies: Grants: Janssen-Cilag and Pfizer. Speaker: Bristol-Myers-Squibb, Eli Lilly, Glaxo-Smith-Kline and Janssen-Cilag.

Dr. Bobes has received research grants and served as consultant, advisor or speaker for the companies: AB-Biotics, Adamed, Almirall, AstraZeneca, Bristol-Myers Squibb, Ferrer, Glaxo- Smith-Kline, Hoffman La Roche, Janssen-Cilag, Lilly, Lundbeck, Merck, Novartis, Organon, Otsuka, Pfizer, Pierre-Fabre, Sanofi-Aventis, Servier, Shering-Plough and Shire, research funding from the Spanish Ministry of Economy and Competiveness –Centro de Investigación Biomedica en Red area de Salud Mental (CIBERSAM) and Instituto de Salud Carlos III-, Spanish Ministry of Health, Social Services and Equality - Plan Nacional sobre Drogas- and the 7th Framework Program of the European Union.

Dr. Garcia-Portilla has been a consultant to and/or has received honoraria/grants from Alianza Otsuka-Lundbeck, Angelini, CIBERSAM, European Comission, Instituto de Salud Carlos III, Janssen-Cilag, Lundbeck, Otsuka, and Pfizer.

Dr. Gutiérrez-Rojas has been speaker for and advisory board member of Bristol-Myers Squibb, Janssen-Cilag, Astra-Zeneca, Rovi, Lundbeck, Otsuka, GSK and Pfizer.

Dr. Martinez-Arán has served as speaker or advisor for the following companies: Bristol-Myers Squibb, Otsuka, Lundbeck and Pfizer.

Dr. Sáiz has been a consultant to or has received honoraria or grants Adamed, AstraZeneca, Brainpharma, Bristol-Myers Squibb, CIBERSAM, Esteve, European Comission, Ferrer inCode, GlaxoSmithKline, Instituto de Salud Carlos III, Janssen-Cilag, Lilly, Lundbeck, Otsuka, Pfizer, Plan Nacional Sobre Drogas, Rovi y Servier.

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Salagre, Cristina Varo, Victoria Ruiz, Carla Torrent, Imma Torres, Anna Giménez, Jorge A. Cervilla and Benedikt L. Amann declare no conflict of interest related to this manuscript.

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