**JAD review**

Recommendation: Reject

Comment: I commend the authors for selecting such a relevant study topic. While there is increasing literature on the individual role of anxiety and trauma, less is known about the mediating/moderating importance of anxiety and trauma on the progress of the bipolar disorder. Unfortunately, the validity and interpretation of the current findings are limited by a number of methodological inaccuracies. The authors should restructure their paper providing a more detailed description of their methodology, better rationale for selecting the variables included in the composite severity score, better discussion of the temporal link between anxiety, trauma and bipolar, and addition of literature related to genetic correlates of anxiety/bipolar disorder, and link between stress response (e.g. HPA) and neural alterations.

Introduction:

* Additional information on the authors’ previous paper (Pavlova et al. 2016 in JAD) should be provided. Since the sample is apparently the same as the one included in the current paper (Pavlova et al. 2015, published in JAD) this should be explicitly stated (both in the introduction and abstract). It would also be important to explain the additional contribution of the current paper when compared to the previous one.
* Please specify if the papers on bipolar disorder the authors referred to (second paragraph) included/excluded child trauma when looking at bipolar and anxiety disorders.
* When referring to previous findings please more specific as to what kind of child maltreatment you are referring to (physical, emotional, neglect). It would also be important to explain why you focus on the total CTQ scores only.
* When you use the words ‘link” and “association” (for instance in reference to Pavlova et al. 2016 on page 2 of your introduction) please specify how this was found (e.g. regression, correlation, path analysis etc.).
* Introduction does not address the following concepts: concept of CTQ (importance of subscores, denial, why self-report vs clinician administered scale evaluating severity of trauma), methods previously used to evaluate trauma, description of the variables included in your bipolar severity index (age, number of mood episodes, hospitalizations, unemployment etc.)
* There is a lack of references referring tothe link between childhood trauma and anxiety disorders in general.

Method

* Include N of participants, age, gender, inclusion and exclusion criteria in your first paragraph describing the sample. Provide rationale as to why you did not include BD-NOS.
* Why did you include all types of anxiety? Are they all related to BD?
* Add subheading to facilitate reading comprehension. E.g. screening, CTQ, Anxiety, severity index
* Authors mention the CTQ subscores but do not use them in their study. Why?
* Please provide a rationale for the selection of the variables in the composite score. Also, I think that rating selected variables on a binary scale lead to information loss, oversimplifies the concept of severity, and limits the relevance of this score. Have the authors thought of using other methods, e.g. regression-based scores aka conducting a factorial analysis, determining how variables loads on each factor and then creating a score from this. I struggle to see the relevance and clinical meaning of this score.
* Can the authors clarify if child trauma occurred prior to the onset of BD? And provide same data for anxiety?
* I would also recommend that the authors provide multicollinearity and correlations scores between the variables included in the composite score.
* As part of the regression it would be important to determine the role of demographic variables such as age and gender, and clinical measures such as severity of manic/depressive episodes, age of onset of the disorder etc. in predicting the severity of the disorder. For instance you could use sequential regression (entering a block of demographic variables) to see if these demographic variables predicted the severity index.
* Statistical analyses: please mention what kind of exploratory analyses you conducted (distribution of data, handling of missing data and outliers).
* Please provide information on medication status of patients and how this was handled in your analyses
* Statistical threshold is not mentioned
* Please provide an estimate of apriori or post-hoc power analysis (alternatively reference to N of subjects vs N of variables included in the regression)
* When authors say “the remaining three items are not scored” (in relation to CTQ) please precise that those 3 items are associated with the denial score
* In addition, not controlling analysis with denial score may bias the results.
* Why conducting analyses with only the total CTQ score?

Results

* Please provide table with the following pieces of information: age, gender, education, employment, medication, comorbidities, IQ estimate, current mood, onset of disease, N hospitalizations, N mood episodes, CTQ total/subdimension scores.
* Did you measure anxiety using STAI etc.? did you consider the concept of anxiety trait vs state? Please discuss
* What does a total CTQ score of 46.2 mean in term of severity? The CTQ manual don’t provide any cut-off score for the total score, only for subscores associated with specific abuse and neglect. Furthermore, the CTQ manual indicates that: “*Studies indicate that the magnitude of a CTQ scale total score is influenced by several dimensions of maltreatment experiences, including their severity, frequency and duration (Fink et al., 1995) …*”. So, analyses solely based on CTQ total score are extremely restrictive..

Not clear when you say “Anxiety disorders were associated with the overall severity index in the sample …” Do you mean number of anxiety disorders? If not, please define this variable.

Discussion

* Since anxiety and trauma estimates were not included in the same regression I wonder if concluding that anxiety is a more powerful predictor than trauma is justified. How do you really compare these concepts?
* Please refer to some biological or neural literature linking to anxiety, trauma, HPA and bipolar, fMRI.
* What about stress and glucorticoid response in anxiety, stress, and bipolar disorder? I think you should include more references to more neural/biological literature (and the increasing body of literature in this field suggests that this may of relevance and of therapeutic interest).
* Although the current findings could indeed have therapeutic relevance I think it would be more relevant to shorten the paragraph on current therapeutic approaches and rather focus on how current findings could be integrated in current approaches.
* Overall, interpreting the results based on the onset of the anxiety disorder vs onset of BD vs at what age individual experienced trauma would be extremely important to understand these findings.
* Please provide references for the following sentence: “Second, anxiety could contribute to sleep disruption and hence mood instability.”
* When it comes to limitations, it should be mentioned that CTQ, being a retrospective self-report applied to an adult population in the present study, is prone to recall bias.
* The sample is not that modest per se. The authors should clarify if it’s modest for the type of analyses they performed. Alternatively, how large should the sample size have been?
* Table 1. please provide exact means, standard deviations, % missing data per variable, ranges of max and minimum for each variable
* Table 2. if rounded to two decimal places the overall severity index is equal to p=.05. this makes me wonder about the significance threshold selected for this study
* Table 4. were the anxiety types categorized as binary variables? (absence or presence of the disorder?).

Technical comments:

* Introduction: authors should provide national statistics (e.g. CDC, NAMI) of suicide and loss of disability-adjusted life years. This kind of statements are more specific and compelling.
* Abstract should contain information on type of BD, remission, age group, gender. Authors could be more specific in relation when they talk of “severity index” as they mean “BD severity”. They should be more specific in terms of predictors and predicted variables. Conclusions should be concise and more specific to the meaning of current findings. A word of advice. Abstract is way too similar to Pavlova et al.’s 2016 abstract. The authors should be more specific about the contribution of the current paper vs their previous one.
* Typo: introduction, second paragraph: “population: Almost…” should be either . Almost..”.