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Prof. Dr. Jin-Xin Kong
Editor
World Journal of Psychiatry

Ribeirão Preto, São Paulo, Apr 27, 2016

Re: 25343- CHRONIC PELVIC PAIN, PSYCHIATRIC DISORDERS AND EARLY EMOTIONAL TRAUMAS: RESULTS OF A CROSS SECTIONAL CASE-CONTROL STUDY INVOLVING PREDICTION ANALYSIS

Dear Editor,

We would like to thank you for your feedback regarding the manuscript that we submitted for publication in your journal. We appreciate the comments and suggestions that were included in your appraisal.

In the responses below, we describe the changes that were made to the manuscript, which are highlighted/colored throughout the text using the track changes mode in MS Word to ensure that the manuscript can be easily reassessed.

We hope that we have sufficiently addressed the comments and suggestions from the reviewers.

Respectfully Yours,

Flávia de Lima Osório

A description of the changes that were made to the manuscript according to the suggestions from the reviewers is as follows:

Reviewer 2445242

Abstract

1. The current Major Depressive Disorder and the Affective Bipolar Disorder emerged as CPP risk factors (ODDS = 5.25 and 9.0). Should be bipolar disorder

Ans: OK! We correct this point in abstract.

2. Conclusions: the findings reinforce the link between mood changes and CPP. Shouldn't this be mood disorders since the association was with MDD & BD?

Ans: OK! We correct this point in abstract.

Introduction

3….moreover, it is not necessary to show the symptoms for more than six months if the patient presents evident signs of central sensitization. This line from the IASP definition needs to be explained.
Ans: OK. We have added a sentence briefly explaining this phenomenon. The central sensitization is an important event in patients with chronic pain. There is no pathognomonic clinically signals or symptoms. Nevertheless, primary or secondary hyperalgesia, dynamic tactile allodynia, the temporal summation of pain are some of them. When these conditions were presented, the chronicity can be considered before six months. Ref: Clifford J Woolf. Central sensitization: Implications for the diagnosis and treatment of pain. Pain. 2011 March ; 152(3 Suppl): S2–15. doi:10.1016/j.pain.2010.09.030.

Results

4. It is highlighted that the cause of CPP is associated to endometriosis in 48% of the participants in the CPP group (N=24), whereas the other participants presented other causes to it such as myofascial syndrome,

irritable bowel syndrome and pelvic inflammatory disease. I couldn't quite understand this part. Does it mean that CPP was associated with endometriosis in the CPP group or the underlying cause(s) of CPP was/were associated with endometriosis? How can the authors state that endometriosis caused CPP when what they found was an association, not a causal relationship? If the etiology of CPP is complex, and relatively unknown how can the authors talk about causes of CPP?

Ans: OK. We agree that the sentence was confused. After a meeting, we decide just list the diagnosis. We add this at the "Results" section.

5. With regards to Axis I psychiatric disorders, there was prevalence of current Major Depressive Disorder among CPP women (Table 3). Shouldn't this be stated as: there was a significantly higher prevalence of major depressive disorder among women with CPP compared to healthy controls?

Ans: Yes, we agree with the reviewer and change the text.

6. There was a general trend to Mood Disorder prevalence in the CPP group. I expect the authors mean that the combined mood disorder diagnoses were higher among the women with CPP, but this is not shown in table 3.

Ans: we showed this information in table 3 – "any mood disorder (p=0.06)". We computed in this category the presence of at least one disorder.

Discussion

7. The authors seem to suggest that BD emerged as a risk factor for CPP because of its link with endometriosis. But they acknowledge that 'analysis between groups did not show statistical significance' and 'Prevalence differences were also not observed in the analyses that have considered the presence or absence of endometriosis.' Moreover, they present no data to show the rates of psychiatric disorders in women with CPP & endometriosis versus women with CPP but without endometriosis. Thus, we are left without

a proper explanation why BD emerged as a risk factor for CPP in the present study.

Ans: Although the difference between the groups regarding the presence of bipolar disorder have not been significant in the univariate analysis, in the multivariate analysis this difference obtained such significance. Thus, there was a higher probability of occurrence of this condition in the CPP group. The reason for this association is found in the studies of Kumar et al, Lewis et al and Walker et al. See page 9/10

8. The authors remark that the association between EET & CPP is confounded by methodological problems and seem to suggest that such an association did not emerge in their study because of it had a different design from earlier studies. Firstly, it is not clear which factors in the EET part of their study-design were different from other studies. Secondly, would the authors consider that some aspects of their study e.g. inadequate powercould have prevented an association to emerge?

Ans: The difference in our study-design is describe in discussion – line 5 :" **However, the present study advances towards the knowledge about this association since it uses a gold standard diagnostic interview and a control group paired by age, school level and economic status to set the presence of depressive disorders"** and in page 5 line 3, when we show the rationale of the study.

General

9. The phrase 'CPP women" should not be used. Use 'women with/suffering from CPP' instead.

Ans: Ok! We chance this term in text

10. The manuscript needs language editing & proper formatting of text

Ans: The text was reviewed by experts in English. Formatting has also been revised

Reviewer 2445281

11. Authors did a very well designed and analyzed study about the presence of chronic pelvic pain and affective disorders. The experimental design and statistical analysis is also appropriated, and the results are clear and concise. There are some problems with the discussion, since in coincidence with authors both processes frequently appear together, but it is hard to accept a cause-effect relationship. It could be better if the authors take one position or other and explain their reasons clearly in the conclusion section. After all, both positions are expressed along the discussion section, but any conclusion is missed.

Ans: Thanks for your comments. We agree, and change the discussion and objective of the study about this - now, we used the association between these situations in function of the probability off occurrence. We change this in title too. In relation to have a positioning, see page 9.

Reviewer 2445205

I have a number of concerns with the paper in its current form. I detail these below in no particular order.

12. A concern with the size of CPP sample. There are only fifty women with CPP and might has high possibility to get false positive or negative results about statistical analysis for prevalence in this study. The authors should provide the evidence of evaluating the sample size, and also a power analysis should be provided in the method section.

Ans: We included analyses about effect size in table 2 and in text

13. The criterion of inclusion and exclusion of CPP in the study should be described more clearly in method section.
Ans: OK. We rewrite this more clearly in “Method" section. We add the follow sentence: "Eligibility criteria were defined as following: chronic or persistent pain perceived in the pelvis-related structures (digestive, urinary, genital, myofascial or neurological system). In this study we have included

just women in reproductive age with acyclic pain and duration equal or greater than six months."

14. In the part of date analysis, the authors chosen these variables whose p value was lower than 0.20 in the group comparison analysis as the independent variables, the authors need to tate the theoretical support for the cut-off value.

Ans: we included two references about this support.