Round-1

Comments to the Author

Reviewer #1:

This paper presented the psychological characteristics of patients with panic related to bipolarity. The authors found that the group of panic disorder with bipolarity (BP+) were more likely to be unmarried and younger, and had higher scores on some psychological assessment scales, such as the MMPI, TCI, BDI, and STAI compared to the group of panic disorder without bipolarity (BP). Logistic regression analysis showed that BP+ group was positively associated with current manic symptoms and trait anxiety, MMPI (Ma) and STAI (trait), and negatively associated with current depressive symptoms. The paper is well written, and the findings are interesting, However, there are still some issues and questions to be answered by the authors.

1. The first main problem of this article is lack of inclusion criteria and exclusion criteria of the participants, and it is unclear whether other factors influence the findings of the patient with panic disorder in the present study. The author should provide these information including illness onset, episodes and treatment.

Answer)
We have already stated that newly diagnosed, consecutive panic disorder patients were included. As you recommended, we described the exclusion criteria of the participants. A. We added this in the 1st paragraph in the Methods section of the paper.

2. The second concerns is about the usage of Mann-Whitney test and Spearman's rank correlation analysis in continuous variables including psychological scale scores. The author should explain the rationality of using these statistical methods.

Answer)

Thank you for your kind comment. The Kolmogorov–Smirnov test did not show a normal distribution of variables in the participants. Therefore, Mann-Whitney test and Spearman's rank correlation analysis were used to analyze the data. We added this explanation in the Statistics section of our paper.

3.The authors presented that the Age, MMPI, TCI, STAI might be the psychological predictors of bipolarity in panic disorder. However, it is interesting and worthy to investigate how the interaction of these psychological characteristics influence the panic disorder. So further analysis including intermediary analysis are encouraged.

Answer)

Thank you for your valuable comment. It is true that there is a possibility of influence due to the interaction of other psychological characteristics. We additionally conducted the Spearman's rank correlation analysis between such variables and the result is shown in the supplementary table.

Reviewer #2:

Specific Comments to Authors: In this study, the authors tried to predict bipolarity in panic disorder patients through simple self-report questionnaires. The included 254 patients with panic disorder. They defined bipolarity as a score of ≥7 on the Korean version of the Mood Disorder Questionnaire (K-MDQ). They used self-report questionnaires to analyze association with bipolarity. Psychological tests included the Mood Disorder Questionnaire (MDQ), Panic Disorder Severity Scale (PDSS), Beck Depression Inventory (BDI), State-Trait Anxiety Inventory (STAI), Temperament and Character Inventory (TCI), and Minnesota Multiphasic Personality Inventory (MMPI). They found that bipolar panic disorder patients were more likely to be unmarried and

younger and had significantly higher scores on the MMPI (Hs, Pd, Mf, Pt, Sc, and Ma), TCI (NS, HA, ST), BDI, and STAI (state and trait) than patients without bipolarity. In logistic regression analysis, MMPI (D), MMPI (Pa), and age were negatively associated; however, MMPI (Ma) and STAI (trait) were positively associated with the bipolarity. In addition, bipolarity was positively associated with current manic symptoms and trait anxiety and negatively associated with current depressive symptoms. They concluded that 50% of patients with panic disorder are likely to have hypomanic or manic symptoms, and that specific psychological factors may be used to better detect such patients. This is a nice study with a good design.

Major comments:

1) Small number of patients

Answer)

As you commented it is true that relatively small numbers of participants are included in the present study and it has a limitation of generalizability of the result. We stressed this in the limitation section (6th paragraph) in the Discussion.

2) All scales were self-reported questionnaires

Answer)

Thank you for your comments about using self-reported questionnaires. We are aware of a disadvantage of the self-report test. The patients can over- or under-report their responses compared to their actual symptoms, and the meaning given to one person's questionnaire score could be different from that of others, even if the same score is chosen by everyone. We specified this in the limitation section (6th paragraph) in the Discussion.

3) No correction of the P value although the authors used different scales and different

comparisons (i.e. multiple testing)

Answer)

I appreciate your valuable comment about the P value that we used in this paper. Even though we did not use any post-hoc correction of P value (i.e. Bonferroni correction), we consulted a biomedical statistician to confirm the proper statistical method to use in the study. We received the confirmation that P value<0.05 is sufficient to support our result of the study from the statistician. But, we agree with your opinion about this matter, so we stressed this in the limitation section (6ᵗʰ paragraph) in the discussion to reflected your valuable advice.

4) Use of abbreviations without explanations of their meaning

Answer) Thank you for your valuable comment about using unexplained abbreviations in the text. We corrected all the abbreviation in the journal.

5) Some statements are redundant and the text should be shortened

Answer) Thank you for your advice. We revised the manuscript to delete unnecessary and redundant sentences from the text.

Specific comments:

1. Abstract: Please provide the full names for these abbreviations in the Abstract: (Hs, Pd, Mf, Pt, Sc, and Ma), (NS, HA, ST), (D), (Pa), (Ma)..

Answer) As you recommended we corrected abbreviations.
'hypochondriasis (Hs), psychopathic deviate (Pd), masculinity-feminity (Mf), psychasthenia (Pt), schizophrenia (Sc), and hypomania (Ma) in MMPI, and novelty seeking, harm avoidance and self-transcendence in TCI, and STAI (state and trait)'

We inserted explanations of abbreviations in the results part of the abstract section.

2. Introduction: there are a lot of repetitions, please shorten them: i.e. "It is well known that there is a strong link between panic disorder and bipolar disorder. Previous studies have shown that patients with bipolar disorder have a high risk of comorbid panic disorder.[1]" and "Panic disorders frequently occur with affective disorders, particularly bipolar disorder." It was already stated in the Introduction!!

Answer) Thank you for your comment about repetitive sentences. As you recommended, we have deleted unnecessary sentences from the 1st paragraph of introduction section.

Deleted sentences: "It is well known that there is a strong link between panic disorder and bipolar disorder." and "Panic disorders frequently occur with affective disorders, particularly bipolar disorder."

3. Introduction: please change this statement: "Birmaher et al. found that youths with panic disorder or bipolar disorder are likely to co-occur with other psychological disorders." Youths do not co-occur! The statement should be written: "Birmaher et al. found that panic disorder or bipolar disorder are likely to co-occur with other psychological disorders in youths."

Answer) Thank you for your correction of the sentence. We've changed the sentence into "Birmaher et al. found that panic disorder or bipolar disorder are likely to co-occur with other psychological disorders in youths."

4. Introduction: please provide appropriate citations for these statements: "Many previous studies have discussed the prognosis of bipolar disorder in the presence of

panic disorder, and few studies have investigated bipolarity in patients with panic disorder."

Answer)

Thank you for your advice. We added citations for the sentence as below.

"Previous studies have discussed the prognosis of bipolar disorder according to the presence of panic disorder, however, few studies have investigated bipolarity in patients with panic disorder. "

5. Methods: Please provide all explanations (in full text) for the abbreviations used in the the MMPI . What is D??

Answer)

As you recommended we corrected abbreviations.

"It contains 10 clinical subscale to evaluate personality and psychopathology of patients: hypochondriasis (Hs), depression (D), hysteria (Hy), psychopathic deviate (Pd), masculinity-feminity (Mf), paranoia (Pa), psychasthenia (Pt), schizophrenia (Sc), hypomania (Ma), and social introversion (Si)."

6. Result should be Results??

Answer)

Thank you for your correction. We changed "Result" into "Results" in Results section of the paper.

7. Add "and"; and replace "than" with "compared to" in this statement: "BP+ group consisted of younger age group (30.78±0.59 versus 37.11±3.21) at the time of the psychological evaluation, and were either unmarried or divorced (single 56.2% versus 44.4%, P = 0.008) compared to BP-group (Table 1).

Answer)

Thank you for your correction of the sentence. We've changed the sentence into "Patients in the BP+ group were younger (30.78±0.59 versus 37.11±3.21) at the time of the diagnosis and were either unmarried or divorced (single 56.2% versus 44.4%, P=0.008) compared to patients in the BP-group. (Table 1)" as you recommended.

8. Please change this statement" In addition, some TCI dimensions of the BP+ group had significantly different scores than those of the BP group." Into "In addition, BP+ group had significantly different scores in some TCI dimensions than BP- group."

Answer)

Thank you for your correction of the sentence. We've changed the sentence into "In addition, BP+ group had significantly different scores in some TCI dimensions than BP- group. Compared to BP- group, BP + group had higher novelty seeking, harm avoidance, and self-transcendence scores, and lower self-directedness and cooperativeness scores." as you recommended.

9. Please add "Compared to BP-group" before these statements: "The BP+ group had higher novelty seeking (NS), harm avoidance (HA), and self-transcendence (ST) scores, and lower self-directedness (SD) and cooperativeness (C) scores. Moreover, the BP+ group also showed higher levels of depressive symptoms as measured by the BDI (31.5 versus 21, P<0.001), and anxiety symptoms measured by STAI (state) and STAI (trait) (state: 63 versus 57, P<0.001 / trait: 61.5 versus 51.5, P<0.001)" This description should be written like this and please delete italics from the p values: "Compared to BP-group, BP+ group had higher novelty seeking (NS), harm avoidance (HA), self-transcendence (ST) scores, lower self-directedness (SD) and cooperativeness (C) scores, higher levels of depressive symptoms as measured by the BDI (31.5 versus 21, P<0.001), anxiety symptoms measured by STAI (state) and STAI (trait) (state: 63 versus 57, P<0.001 / trait: 61.5 versus 51.5, P<0.001)."

Answer)

Thank you for your correction on the sentence. We changed the sentence into below as you recommended.

"Compared to BP- group, BP + group had higher novelty seeking, harm avoidance, and self-transcendence scores, and lower self-directedness and cooperativeness scores. Moreover, the BP+ group also showed higher levels of depressive symptoms as measured by the BDI (31.5 versus 21, $P<0.001$), and anxiety symptoms measured by STAI (state) and STAI (trait) (state: 63 versus 57, $P<0.001$ / trait: 61.5 versus 51.5, $P<0.001$) (Table 2)."

10. Please delete a dot before the pa value: "K-MDQ scores were negatively associated with years of education and TCI self-directedness dimension scores ($P<0.05$).

Answer)

Thank you for your comment. We deleted a dot before P-value.

11. In the Results, please provide explanations for these abbreviations: "In correlation analyses (Table 3), K-MDQ scores were associated with increasing MMPI HS, D, Pd, Mf, Pa, Pt, Sc, Ma, Si clinical scales…"? Also, under Tables 2, 3 and 4, provide explanations for the abbreviations.

Answer)

Thank you for your comment about using inappropriate abbreviations. We explained all the abbreviations in the results section and under the table 2,3 and 4 in the paper.

A corrections made in the results section: "In correlation analyses (Table 3), K-MDQ scores were associated with increasing hypochondriasis (Hs), depression (D), psychopathic deviate (Pd), masculinity-feminity (Mf), paranoia (Pa), psychasthenia

(Pt), schizophrenia (Sc), hypomania (Ma) and, social introversion (Si) in MMPI clinical scales, TCI novelty seeking, harm avoidance and self-transcendence dimensions, and higher BDI, STAI (state), and STAI (trait) scores."

12. The same comment applies here: "In correlation analyses (Table 3), K-MDQ scores were associated with increasing MMPI HS, D, Pd, Mf, Pa, Pt, Sc, Ma, Si clinical scales…" What are these abbreviations: HS, D, Pd, Mf, Pa, Pt, Sc, Ma, Si??

Answer)
Thank you for your valuable comment about the abbreviations. We changed the abbreviations into explanations as below.

A corrections made in the results section: "In correlation analyses (Table 3), K-MDQ scores were associated with increasing hypochondriasis (Hs), depression (D), psychopathic deviate (Pd), masculinity-feminity (Mf), paranoia (Pa), psychasthenia (Pt), schizophrenia (Sc), hypomania (Ma) and, social introversion (Si) in MMPI clinical scales, TCI novelty seeking, harm avoidance and self-transcendence dimensions, and higher BDI, STAI (state), and STAI (trait) scores."

13. Discussion: The authors stated that: "The aim of this study was to find the difference in demographic characteristics and various clinical symptoms between the panic disorder group with and without a high risk of being diagnosed with bipolar disorder, to find the variable that can predict the potential risk of bipolar disorder in patients with panic disorder." First, the aim of the study goes into Introduction. Second, they included subjects with panic disorder with and without bipolar disorder (according to the criteria they described in Methods ("Patients with scores above the threshold score of 7 were considered as patients with bipolarity (BP+ group) and the remaining were considered as patients without bipolarity (BP– group).", and not "the panic disorder group with and without a high risk of being diagnosed with bipolar

disorder".

Answer)

Thank you for your valuable comments. We repositioned the aim of the study into the 3rd paragraph of the Introduction section. Also as you recommended, we clarified the aim of the study.

14. Discussion: What did the authors wanted to state here: "Among the 254 subjects who were diagnosed with panic disorder, approximately 50% the patients scored 7 or more on the K-MDQ, suggesting a history of manic/hypomanic symptoms in the past. As a result, the younger the diagnosis, the higher the risk of bipolarity"?? The statement "As a result.." is wrong; the authors found with a correlation that younger age was significantly associated with an increased K-MDQ score (BP+ group)." Therefore, these statements should be written (without "as a result" part), like this: "Younger age was associated with the higher the risk of bipolarity, while the manic subscale of the MMPI, and the STAI (trait) score, which indicates the innate anxiety level, were positively related to the bipolarity in panic patients. "

Answer)

Thank you for your valuable advice. We changed the sentence as you suggested.
Corrected sentence: "Younger age and the hypomanic (Ma) subscale of the MMPI were associated with the higher risk of bipolarity. In addition, the STAI (trait) score, which indicates the innate anxiety level, is positively related to the bipolarity of panic patients, while the self-directedness score in the TCI was negatively associated."

15. When the authors state "In previous studies..", more than one citations should be given. If they cite only one study, the statement should be corrected, but the authors should comment: "In line with our data, in a previous study, early age at onset of

panic disorder was associated with an increased morbidity risk for bipolar comorbidity.[27]"

Answer)

Thank you for your comment about the citations. We corrected the stated as you recommended.

Corrected sentence: "In line with our data, in a previous study, an early age at onset of panic disorder was associated with an increased morbidity risk for bipolar comorbidity.(29)"

16. The same comment applies here: "Moreover, previous studies have already shown that the risk of anxiety disorder increases as the onset age of bipolar disorder decreases.[30]" It should be: "Moreover, a previous study has already shown that the risk of anxiety disorder increases as the onset age of bipolar disorder decreases.[30]"

Answer) Thank you for your comment. We changed the sentence as you recommended.

Corrected sentence: "Moreover, a previous study has already shown that the risk of anxiety disorder increases as the onset age of bipolar disorder decreases.(31)"

17. Please correct this statement: "It was found that patients with panic disorder with bipolarity had a positive correlation and the panic disorder patients without bipolarity had a negative correlation with the manic subclinical score." Patients do not have a positive or negative correlation!! The authors have found that : "Manic subclinical scores were positive correlated with bipolarity in patients with panic disorder with bipolarity, and were negative correlated with bipolarity in patients without bipolarity."

Answer)

Thank you for your valuable comment. We changed the sentence into "In our study, it was found that MMPI hypomanic subscale scores were positively correlated with bipolarity in patients with panic disorder. The result of this study was consistent with previous studies, stating that the high score of hypomanic subscale is indicative of diagnosis of bipolar disorder. (35, 36)"

18. Please provide citation: "Many studies have identified bipolarity in patients with anxiety or depression."

Answer) We appreciate your advice. We decided to delete "Many studies have identified bipolarity in patients with anxiety or depression." Because this sentence was not closely related to the subject of this paragraph.

19. This is redundant: "Several tests and analysis tools have been developed to help diagnose psychiatric patients."

Answer) We appreciate your advice. As you mentioned, we corrected the sentence to avoid redundancy.

Corrected sentence: "Several psychometric tests have been developed to help diagnose psychiatric patients and the MMPI is one of the most commonly used standardized psychometric tests of adult personality and psychopathology.(33)"

20. Please delete "natural" from: "In addition, patients with panic disorder and bipolarity felt less depressed compared to patients without bipolarity, which is a natural result considering the nature of bipolar disorder manic symptoms. " it should be corrected into: "In addition, patients with panic disorder and bipolarity felt less depressed compared to patients without bipolarity, which results from the nature of

bipolar disorder manic symptoms. "

Answer)

Thank you for your correction. We corrected the sentence as you recommended.

Corrected sentence: "In addition, patients with panic disorder and bipolarity felt less depressed compared to patients without bipolarity, which results from the nature of bipolar disorder manic symptoms."

21. Singular (not studies, study when you cite only one reference): "However, previous studies focusing on the relationship between temperament and panic disorder, high scores of harm avoidance (HA), and reward dependence (RD) are related to panic symptoms.[36] please correct into: "However, previous study focusing on the relationship between temperament and panic disorder, high scores of harm avoidance (HA), and reward dependence (RD) are related to panic symptoms.[36]"

Answer)

Thank you for your comment. We changed the sentence as you recommended.

Corrected sentence: "In addition, a previous study focusing on the relationship between temperament and panic disorder, high scores of harm avoidance, and reward dependence were related to panic symptoms.(38)"

22. Again, patients are not positively correlated; their scores are correlated: "Patients with panic disorder and high levels of anxiety are positively correlated with bipolarity, particularly when having anxious characteristics." Correct into: "High levels of anxiety were positively correlated with bipolarity, particularly when having anxious characteristics in patients with panic disorder."

Answer) Thank you for your valuable correction in grammatical errors. We corrected the sentence as you recommended.

Corrected sentence: "High levels of anxiety were positively correlated with bipolarity, particularly when having anxious characteristics in patients with panic disorder."

EDITORIAL OFFICE'S COMMENTS

(1) Science editor: 1 Scientific quality: The manuscript describes a retrospective study of the psychological predictors of bipolarity in panic disorder. The topic is within the scope of the WJP. (1) Classification: Two Grades B; (2) Summary of the Peer-Review Report: In this study, the authors tried to predict bipolarity in panic disorder patients through simple self-report questionnaires. The paper is well written, and the findings are interesting. The questions raised by the reviewers should be answered; (3) Format: There are 4 tables; (4) References: A total of 41 references are cited, including 6 references published in the last 3 years; (5) Self-cited references: There is no self-cited reference; and (6) References recommendations: The authors have the right to refuse to cite improper references recommended by the peer reviewer(s), especially references published by the peer reviewer(s) him/herself (themselves). If the authors find the peer reviewer(s) request for the authors to cite improper references published by him/herself (themselves), please send the peer reviewer's ID number to editorialoffice@wjgnet.com. The Editorial Office will close and remove the peer reviewer from the F6Publishing system immediately. 2 Language evaluation: Classification: Two Grades B. A language editing certificate issued by Editage was provided. 3 Academic norms and rules: The authors provided the Biostatistics Review Certificate, the Institutional Review Board Approval Form. Written informed consent was waived. No academic misconduct was found in the Bing search. 4 Supplementary comments: This is an invited manuscript. No financial support was obtained for the

study. The topic has not previously been published in the WJP.

5 Issues raised

(1) The "Article Highlights" section is missing. Please add the "Article Highlights" section at the end of the main text.

Answer)

Thank you for your advice. We included the "Article Highlights" at the end of the main text.

(2) Editorial office director: **none**

(3) Company editor-in-chief: I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Psychiatry, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors.

Round-2

Comments to the Author

Specific comments to authors

Statistics. Please remove „between" / two times was written/ from: „Kolmogorov-Smirnov test determined whether the data were normally distributed. The Mann-Whitney and chi-square test was conducted to compare demographic and clinical variables between between the group with an MDQ score of less than 7 and the group with an MDQ score of 7 or more (BP+ group)."

Answer) Thank you for your correction of the sentence. We deleted redundant

"between" in the sentence in Statistics section of our paper.

Corrected sentence: The Mann-Whitney and chi-square test was conducted to compare demographic and clinical variables between the group with an MDQ score of less than 7 and the group with an MDQ score of 7 or more (BP+ group).

Discussion: ad „in" in this sentence: „In addition, in a previous study focusing on the relationship between temperament and panic disorder, high scores of harm avoidance, and reward dependence were related to panic symptoms.(38)"

Answer) Thank you for your correction. As you recommended, we added "in" in the sentence in Discussion section.

Corrected sentence: In addition, in a previous study focusing on the relationship between temperament and panic disorder, high scores of harm avoidance, and reward dependence were related to panic symptoms.

Limitation: Please reformulate this statement, it is not clear what the authors wanted to state??:" However, the study design is may related to the selection bias and hinder the generalizability of the results". Presumably the authors should delete "is" and add "be": However, the study design may be related to the selection bias and hinder the generalizability of the results."

Answer) Thank you for your correction. As you recommended, we corrected the sentence in Limitation section.

Corrected sentence: However, the study design may be related to the selection bias and hinder the generalizability of the results.