Reviewer’s report

Title: Variation in the CACNB2 Gene is Associated with Functional Connectivity of the Hippocampus in Bipolar Disorder

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Reviewer: Sergi Papiol

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Manuscript ID BPSY-D-18-00864
Title: Variation in CACNB2 Gene is Associated with Functional Connectivity of the Hippocampus in Bipolar Disorder

Authors: Liu F et al.

This is a very interesting study carried out on a Chinese cohort of bipolar disorder patients (N=69) and healthy controls (N=133) with neuroimaging and genomic data available. The authors evaluated the influence of rs11013860 genotype in CACNB2 gene on resting-state functional connectivity. The authors identify some suggestive genotype-dependent effects in several brain regions.

The study is interesting, and the results are suggestive. However I have some questions/remarks:

Comments for authors:

Abstract:

- rs11013860 is the ID for a single nucleotide polymorphism but nor for CACNBs. Please correct.

- The results are confusing in their current form. Please correct.

- As a general comment I would suggest a correction of English throughout the whole text.

Introduction:

- What is the exact significance (P-value) of rs11013860 in the CACNB2 gene in the mentioned GWAS in Han Chinese population (reference 4).

- Has rs11013860 any known functional effect on expression? Where is it located, promoter/regulatory regions? Exons? Please specify.

- Please be more specific on the observed effect of CACN2B SNPs mentioned in references 8, 9, 10.
Methods:
- What is the rationale to group subjects as CC versus A-carriers? Not really clear why this has been done.
- Was there any power analysis done before doing analyses?

Results:
- It's difficult to understand which are the areas showing differences in each analysis. Please rewrite the whole results section for clarity.

Discussion:
- I would suggest significantly shortening (to half the current length) the discussion section but keeping the current concepts.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Unable to assess

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

Quality of written English
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

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