Reviewer’s report

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

Version: 0 Date: 03 Dec 2018

Reviewer: Giovanni Severino

Reviewer's report:

Dear Editor

The aim of this study is to investigate the role of calcium channel, voltage-dependent, beta 2 subunit gene (CACNB2) on the hippocampus-cortex limbic circuits in patients affected by bipolar disorder (BD). Author use a genetic and functional magnetic resonance integrated approach.

The hypothesis of the study is robust

1) rs11013860 in CACNB2 seems quite relevant in the Chinese population for bipolar illness

2) CACNB2 is predominantly expressed in hippocampal pyramidal neurons and abnormal network connectivity of Hippocampus are implicated in Bipolar Disorder

Authors genotyped 69 bipolar patients and 133 healthy controls for rs11013860 and all participants have been studied with functional magnetic resonance in order to detect altered hippocampus-cortex neuroconnectivity. Result shows that BD patients with CACNB2 rs11013860 AA/CA genotype may demonstrated altered hippocampus-cortex neuroconnectivity.

One concern:

Materials and Methods: clarify how many patients are Bipolar 1 or Bipolar 2 and the mood stabilizer therapy (in particular Lithium). If these data are not available, please put this point as limitation of the study in the Discussion section.

In the complex the study is well conducted, the paper is clear and references complete.

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

Yes

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

**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.

Not relevant to this manuscript

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

Acceptable

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