

## Revisions:

### **A. Response to Reviewers:**

Reviewer 1: *Major Depressive Disorder (MDD) contributes significantly to the global burden of disease. Observations suggest that antidepressants commonly used to treat MDD act by promoting neuroplasticity in depression-relevant brain circuits. Moreover, research on the use of serotonergic psychedelics in depression treatment shows promising results. However, their mechanism of action is still unclear. This article explored what effects the use of serotonergic psychedelics has on markers of neuroplasticity. For this purpose, the literature on the association of depression, antidepressants, and ketamine with changes in neuroplasticity at a molecular, cellular, electrophysiological, functional, structural, and psychological level was reviewed. The authors highlight the role of neuroplasticity in the use of serotonergic psychedelics and provide important suggestions for further research on the use of serotonergic psychedelics in depression treatment. Thank you for this interesting and timely article.*

Thank you for your feedback.

Reviewer 2: *Depression is a common mental disorder and one of the leading causes of disability around the world. Treatment of depression has been an important topic for the clinical research and practice. Early clinical trials are now showing promising results of serotonergic psychedelics for depression; however, their mechanism of action remains poorly understood. This paper reviewed the effect of depression, classic antidepressants, ketamine, and serotonergic psychedelics on markers of neuroplasticity at a cellular, molecular, electrophysiological, functional, structural, and psychological level to explore the potential role that neuroplasticity plays in the treatment response of serotonergic psychedelics. The article are quite important for the clinical practice. However, I have a minor comment. As we all know, ketamine is a component of commonly used anesthetics on the operating table, and is also an addictive drug called "k powder", and many research have reported the side effect of ketamine. However, the authors did not mention about the side effect of the serotonergic psychedelics for depression. So I would suggest the authors add some sentence to describe these briefly.*

Thank you for your feedback. Information regarding the potential negative effects of serotonergic psychedelics has been added in the introduction.

### **B. Response the Science Editor:**

- 1) Author contributions section has been added
- 2) Grant Support Form has been included
- 3) The figure we included is an original we have also included the PowerPoint
- 4) References have been updated
- 5) Figure is original

### **C. Steps for Resubmission**

- 1) Updated Authorship, Institution and Corresponding Author, per Guidelines
- 2) Checked to see that manuscript information is correct
- 3) Updated Manuscript according to guidelines
- 4) Updated References per Guidelines
- 5) Updated Footnotes, Figure and Figure Legend Per Guidelines
- 6) Previewed full text file
- 7) Uploaded the revision files

**D. Uploaded Copyright License Agreement signed by all authors**

**E. Uploaded Conflict of Interest Forms from all authors**