



## PEER-REVIEW REPORT

**Name of journal:** World Journal of Psychiatry

**Manuscript NO:** 65474

**Title:** Glutamate and depression: Reflecting a deepening knowledge of the gut and brain effects of a ubiquitous molecule

**Reviewer's code:** 02445267

**Position:** Editorial Board

**Academic degree:** MD, PhD

**Professional title:** Associate Professor, Doctor

**Reviewer's Country/Territory:** Italy

**Author's Country/Territory:** Nigeria

**Manuscript submission date:** 2021-03-07

**Reviewer chosen by:** Man Liu

**Reviewer accepted review:** 2021-03-09 06:17

**Reviewer performed review:** 2021-03-09 06:42

**Review time:** 1 Hour

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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#### **SPECIFIC COMMENTS TO AUTHORS**

The manuscript 65474 titled "Glutamate and glutamate-based therapies in depression: reflecting a deepening knowledge of the gut and brain effects of a ubiquitous molecule" submitted to WJP is an interesting research chiefly focused on the role of glutamate in depressive disorders. The main findings and conclusion are there is a lack of attention on the role diets containing high concentrations of m glutamate that may increase bodily levels of glutamic acid, thus resulting in hyperglutamatergic neurotransmission, which could possibly contribute to the development of depression. I have the following comments: -In the whole topic is interesting but as a reader it appear to me as not well-coordinated. In the section 1.1.2 Endogenous brain glutamate and depression Authors might add more information on the studies alterations in glutamatergic neurotransmission and depression: such as methodology, study population, tools the primary outcome for each study. The information are often redundant so that I suggest to shortened this version. REFERENCES: THE AUTHORS APPEALED 12 SELF-CITATIONS.



### PEER-REVIEW REPORT

**Name of journal:** World Journal of Psychiatry

**Manuscript NO:** 65474

**Title:** Glutamate and depression: Reflecting a deepening knowledge of the gut and brain effects of a ubiquitous molecule

**Reviewer's code:** 05492281

**Position:** Editorial Board

**Academic degree:** MD

**Professional title:** Consultant Cardiac Surgeon, Neurosurgeon, Research Scientist

**Reviewer's Country/Territory:** China

**Author's Country/Territory:** Nigeria

**Manuscript submission date:** 2021-03-07

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2021-03-08 00:24

**Reviewer performed review:** 2021-03-14 05:07

**Review time:** 6 Days and 4 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input type="checkbox"/> Anonymous <input checked="" type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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## **SPECIFIC COMMENTS TO AUTHORS**

The authors reviewed in detail the endogenous and exogenous sources of glutamate and its relationship with depression. The gut-brain axis is a very important signal regulating axis. Change glutamate homeostasis to affect the incidence of depression. Abnormal function of amino acid neurotransmitters and impaired energy metabolism constitute the pathophysiological basis of severe depression. GLU is currently considered to be the most abundant neurotransmitter in the brain, and its excitability plays an important role in the structure and function of the brain. The regulation of GLU pathway has rapidly become a key target for the development of neuropsychiatric drugs. Future new drugs may regulate the GLU signaling pathway to treat mental and somatic comorbidities, such as schizophrenia comorbid diabetes, depression comorbid body pain. It is worth noting that patients with schizophrenia already have glucose metabolism disorders at the time of onset, which may be due to GLU excitotoxicity in both the body and the brain. The main reason why depression is not easy to cure and easy to relapse is that psychological factors are not removed. Drugs only control some symptoms of the disease, and may relapse when stimulated by psychosocial factors. We should further elaborate on the classification of glutamate receptors, and then focus on the biochemical and pharmacological changes of glutamate receptors induced by antidepressants, as well as the clinical and animal models of glutamate dysfunction.



## PEER-REVIEW REPORT

**Name of journal:** World Journal of Psychiatry

**Manuscript NO:** 65474

**Title:** Glutamate and depression: Reflecting a deepening knowledge of the gut and brain effects of a ubiquitous molecule

**Reviewer's code:** 02804922

**Position:** Editorial Board

**Academic degree:** PhD

**Professional title:** Professor

**Reviewer's Country/Territory:** Mexico

**Author's Country/Territory:** Nigeria

**Manuscript submission date:** 2021-03-07

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2021-03-08 03:25

**Reviewer performed review:** 2021-03-15 06:13

**Review time:** 7 Days and 2 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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## **SPECIFIC COMMENTS TO AUTHORS**

The manuscript presented by Dr. Onalapo presents an interesting review of literature on glutamate participation in major depression and how this knowledge is used to improve the management of major depression through new pharmacological treatments the title is appropriate and adequately reflects the content of the manuscript the abstract is correctly formulated and presents to the reader all the issues addressed in the manuscript The keywords are adequate The review is well planned and presents a broad overview of the role of glutamate in psychiatric conditions, particularly major depression. However, some additions and improvements would further increase the quality of the manuscript. Initially, The authors should correct some minor errors in English. Additionally, the manuscript would deeply enrich by incorporating tables that condense the information on molecules, receptors, and effects with their corresponding bibliographic citations. And one point that I consider essential is the inclusion of a diagram that presents the reader with the molecular steps of glutamate interaction, pointing out its sources, the receptors with which it interacts, and its effects, specifying the site of action of the drugs described. in review Additionally, I consider that the authors must review the number of self-citations in this review. the remaining points adequately comply with what is expected



## RE-REVIEW REPORT OF REVISED MANUSCRIPT

**Name of journal:** World Journal of Psychiatry

**Manuscript NO:** 65474

**Title:** Glutamate and depression: Reflecting a deepening knowledge of the gut and brain effects of a ubiquitous molecule

**Reviewer's code:** 02804922

**Position:** Editorial Board

**Academic degree:** PhD

**Professional title:** Professor

**Reviewer's Country/Territory:** Mexico

**Author's Country/Territory:** Nigeria

**Manuscript submission date:** 2021-03-07

**Reviewer chosen by:** Chen-Chen Gao

**Reviewer accepted review:** 2021-04-14 03:01

**Reviewer performed review:** 2021-04-14 03:35

**Review time:** 1 Hour

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

### SPECIFIC COMMENTS TO AUTHORS



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After reviewing the new version of manuscript ID: 65474, I believe that the requested points have been partially covered. I did not see the Figure 1 mentioned in the paper; in the last revision, this figure was requested. Likewise, and even though two reviewers agree on an excessive number of self-citations in this manuscript. The number of self-citations has only been reduced from 12 to 10, so seven more self-citations should be replaced or removed to have a number less than or equal to 5 self-citations, so I request a new version of this manuscript