



## PEER-REVIEW REPORT

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

**Manuscript NO:** 81826

**Title:** Kynurenine pathway of tryptophan metabolism in pathophysiology and therapy of major depressive disorder

**Provenance and peer review:** Invited manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 05906528

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Assistant Professor, Staff Physician

**Reviewer's Country/Territory:** United States

**Author's Country/Territory:** United Kingdom

**Manuscript submission date:** 2022-11-25

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2022-11-25 16:47

**Reviewer performed review:** 2022-12-04 01:32

**Review time:** 8 Days and 8 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 Grade E: Do not publish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 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



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<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**

With more and more advanced research in the field of treatment resistant depression, the focus of treatment strategies is shifting from the monoamine system to other biological mechanisms. One of such critical systems is the glutamatergic system. The kynurenine pathway plays a critical role in generating cellular energy in the form of nicotinamide adenine dinucleotide. In this pathway, tryptophan is converted into several bioactive molecules including serotonin while majority of it is converted into kynurenine and its breakdown products. The authors have done justice in describing the tryptophan metabolizing enzymes and kynurenine pathway. Through a series of steps kynurenine is converted into quinolinic acid, which has NMDA receptor agonist properties and kynurenic acid, which is an NMDA receptor antagonist. A hypothesis suggests that the competing actions of quinolinic acid and kynurenic acid at the NMDA receptor may play role in inflammation and glutamate models of depression. Ref:Savitz J. The kynurenine pathway: a finger in every pie. Mol Psychiatry. 2020. The authors have discussed the kynurenine pathway underlying MDD pathophysiology and being a target of antidepressant therapy briefly in the last section of the review. May be more focus & elaboration on that instead of the very brief section on role of anti-inflammatory medications such as celecoxib in MDD therapy would improve the quality of this review article and provide higher clinical utility. The tables and figures are helpful.



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**Position:** Peer Reviewer

**Academic degree:** MD, MSc, PhD

**Professional title:** Attending Doctor, Research Assistant Professor

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

**Author's Country/Territory:** United Kingdom

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<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
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<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No



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	Conflicts-of-Interest: [ <input type="checkbox"/> ] Yes [ <input checked="" type="checkbox"/> ] No

### **SPECIFIC COMMENTS TO AUTHORS**

This Review discusses an interesting medical topic. However, there are the following main problems: 1. The author cited too few relevant references, exaggerating the the role of Kynurenine pathway of tryptophan metabolism in pathophysiology and therapy of major depressive disorder. 2. The metabolic pattern diagram is too simple. It is suggested to display it visually for the readers to understand. 3. In the absence of research data support, some personal hypotheses were conducted.