

PEER-REVIEW REPORT

Name of journal: *World Journal of Psychiatry*

Manuscript NO: 76582

Title: Depressive disorder and antidepressants from an epigenetic point of view

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05198253

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Academic Research, Chief Doctor, Doctor, Research Scientist

Reviewer's Country/Territory: China

Author's Country/Territory: Slovenia

Manuscript submission date: 2022-03-25

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-03-27 07:32

Reviewer performed review: 2022-04-01 11:20

Review time: 5 Days and 3 Hours

Scientific quality	<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 Grade E: Do not publish
Language quality	<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
Conclusion	<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
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous



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statements

Conflicts-of-Interest: [] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Overall: Good topic, important conversation, general interest. The authors do a good job of performing a review of the available studies on epigenetic changes in depressive disorder and the effects on antidepressants. This work can be published in WJP after revision. 1. Authors need to add relevant diagrams with reference to the literature, thus increasing the readability of the article. For example: Epigenetic Modifications of Major Depressive Disorder. 2. The article needs to add a prospective section after the conclusion. Give some inspiring points for future research.

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Professional title: Doctor, Postdoc

Reviewer's Country/Territory: China

Author's Country/Territory: Slovenia

Manuscript submission date: 2022-03-25

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-04-02 01:10

Reviewer performed review: 2022-04-02 01:43

Review time: 1 Hour

Scientific quality	<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
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Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous

statements

Conflicts-of-Interest: [] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

In this review manuscript, the authors discussed depressive disorder and antidepressants from an epigenetic point of view. The topic is interesting. Some concerns and suggestions are listed as below: 1. Microglia can be pre-conditioned through epigenetic-driven innate immune memory that persists for several months. Epigenetic alterations of microglia during early life may re-program the communication between microglia and other cells in the CNS and have significant later consequences for behavior and disease. This point should be discussed. Ref: Innate immune memory in the brain shapes neurological disease hallmarks, *Nature*, 2018. 2. From a sex viewpoint, females have been reported to have higher levels of DNA methyltransferase enzyme activity, DNA methylation, and methylated CpG sites than do males in the neonatal POA. Inhibiting DNA methyltransferase causes masculinized neuronal markers and male sexual behavior in female rats, suggesting that DNA methylation serves as the basis for the sex-specific transcriptomes in selective brain regions. This point should be discussed. Ref: Uncovering sex differences of rodent microglia, *Journal of Neuroinflammation*, 2021.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Reviewer's code: 05395205

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Doctor, Postdoc

Reviewer's Country/Territory: China

Author's Country/Territory: Slovenia

Manuscript submission date: 2022-03-25

Reviewer chosen by: Jia-Ru Fan

Reviewer accepted review: 2022-06-15 08:56

Reviewer performed review: 2022-06-15 08:58

Review time: 1 Hour

Scientific quality	<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
Language quality	<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
Conclusion	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Peer-reviewer statements	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

The authors have addressed my concerns.