

## PEER-REVIEW REPORT

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

**Manuscript NO:** 82720

**Title:** Epigenetics in psychiatry: Beyond DNA methylation

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

**Peer-review model:** Single blind

**Reviewer's code:** 02445209

**Position:** Editorial Board

**Academic degree:** N/ A, MD, PhD

**Professional title:** Professor

**Reviewer's Country/Territory:** Czech Republic

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

**Manuscript submission date:** 2022-12-27

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2023-01-02 08:43

**Reviewer performed review:** 2023-01-09 06:17

**Review time:** 6 Days and 21 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 Grade E: Do not publish
Novelty of this manuscript	<input checked="" type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
Creativity or innovation of this manuscript	<input checked="" type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation

<b>Scientific significance of the conclusion in this manuscript</b>	<input checked="" type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
<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 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

## SPECIFIC COMMENTS TO AUTHORS

Dear authors, I have a few comments on your manuscript: - You are rather courageous when you submit a manuscript to the World Journal in Psychiatry not having any psychiatrist in your authors' team at all. I do not doubt your high expertise in molecular genetics, but your knowledge of psychiatry is below-average. On the other hand, I appreciate the topic of your manuscript, which is important and innovative in etiology of mental disorders. - Introduction - Biomarkers and psychiatric disorders - the lines 3 and 4 from above: In psychiatry, diagnoses are made based on psychiatric examination, not on "physical" examination. Not only the Diagnostic and Statistical Manual of Mental Disorders (in America, created by the American Psychiatric Association), but also the International Classification of Mental Disorders ICD-11 (in the rest of the world, created by the WHO) are applied in psychiatric diagnostics. - The readers of the journal are mostly clinical psychiatrists. So the part of your manuscript "Methods for DNA hydroxymethylation detection" will be too uninteresting and unsuitable for them. I suggest you to shorten this part of your manuscript by about a half. - Current overview of DNA hydroxymethylation studies...: Psychiatric disorders (their etiology) are

influenced not only by genetic and epigenetic factors, but also by microbiome, environmental factors and last but not least by their wide interactions, labeled e.g. as GxGxGxExE... - DNA hydroxymethylation and depression: "Depression" is a very broad term usually not used in psychiatric professional articles because of its vagueness. If you use the term "depression", you should always specify it more, e.g. "major depression", "organic depressive disorders", "depression within an adjustment disorder" etc. - Conclusion: I do not agree with the first sentence "In treatment of psychiatric disorders there are currently no validated biomarkers in use". You should know that biomarkers can be not only molecular/genetic ones, but we also have e.g. electrophysiological biomarkers (EEG), neuropsychological biomarkers, brain imaging biomarkers, blood biomarkers etc. For example, in Alzheimer's dementia, brain imaging or the examination of cerebrospinal fluid have already been applied and useful in finding proper biomarkers for the diagnostics and treatment (brain atrophy, tau-protein, beta-amyloid etc.). - Conclusion: You mention that "psychiatric disorders are polygenic". You should also mention that in addition to single nucleotide polymorphisms (SNPs), copy number variations (CNVs), genetic pleiotropy, epistasis etc. play an important role in the genetics of mental disorders. The reviewer

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**Reviewer's code:** 05471835

**Position:** Peer Reviewer

**Academic degree:** Doctor, PhD

**Professional title:** Professor

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

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

**Manuscript submission date:** 2022-12-27

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2022-12-30 20:45

**Reviewer performed review:** 2023-01-11 05:53

**Review time:** 11 Days and 9 Hours

Scientific quality	<input checked="" type="radio"/> Grade A: Excellent <input type="radio"/> Grade B: Very good <input type="radio"/> Grade C: Good <input type="radio"/> Grade D: Fair <input type="radio"/> Grade E: Do not publish
Novelty of this manuscript	<input checked="" type="radio"/> Grade A: Excellent <input type="radio"/> Grade B: Good <input type="radio"/> Grade C: Fair <input type="radio"/> Grade D: No novelty
Creativity or innovation of this manuscript	<input checked="" type="radio"/> Grade A: Excellent <input type="radio"/> Grade B: Good <input type="radio"/> Grade C: Fair <input type="radio"/> Grade D: No creativity or innovation

<b>Scientific significance of the conclusion in this manuscript</b>	[ <input checked="" type="checkbox"/> ] Grade A: Excellent    [ <input type="checkbox"/> ] Grade B: Good    [ <input type="checkbox"/> ] Grade C: Fair [ <input type="checkbox"/> ] Grade D: No scientific significance
<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 checked="" type="checkbox"/> ] Accept (High priority)    [ <input type="checkbox"/> ] Accept (General priority) [ <input 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

## SPECIFIC COMMENTS TO AUTHORS

Contemporary research on DNA hydroxymethylation and psychiatric disorders is particularly significant, especially in the field of suicide, schizophrenia, bipolar disorder, depression, and obsessive-compulsive disorder, as it contributes to elucidating our understanding of the molecular background of psychiatric disorders. In your manuscript, you provided an overview of all studies on this topic and explained the etiology of psychiatric disorders at the molecular level. As a limitation I think that from the aspect of epigenetics, it would be important to investigate personality disorders and addictive diseases that also carry a high risk for suicidal behavior.