

## PEER-REVIEW REPORT

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

**Manuscript NO:** 65781

**Title:** BDNF methylation and mRNA expression in brain and blood of completed suicides in Slovenia

**Reviewer's code:** 02446061

**Position:** Editorial Board

**Academic degree:** MD, PhD

**Professional title:** Full Professor, Research Scientist

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

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

**Manuscript submission date:** 2021-03-16

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2021-03-16 23:26

**Reviewer performed review:** 2021-03-17 22:35

**Review time:** 23 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 Grade E: Do not publish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

## **SPECIFIC COMMENTS TO AUTHORS**

The manuscript content is interesting. The BDNF methylation and psychiatric disorders is an attractive topic. I suggest some changes for consideration. a) I suggest the exclusion of the patient with schizophrenia in the control group. Those in the study group are well, but maybe data from that with PD sounds inadequate as is not a main topic in the content, neither it has been analyzed by statistics tools (very difficult being just one case). b) In methods, check if the mix of samples could be adequate to the analysis. Or argue if this method limit the exclusion of the mentioned patient ( with schizophrenia in control group). c) Several works about BDNF methylation could to help enrich the discussion content: - Perroud, N., Salzmann, A., Prada, P., Nicastro, R., Hoeppli, M. E., Furrer, S., ... & Malafosse, A. (2013). Response to psychotherapy in borderline personality disorder and methylation status of the BDNF gene. *Translational psychiatry*, 3(1), e207-e207. - González-Castro, T. B., Salas-Magaña, M., Juárez-Rojop, I. E., López-Narváez, M. L., Tovilla-Zárate, C. A., & Hernández-Díaz, Y. (2017). Exploring the association between BDNF Val66Met polymorphism and suicidal behavior: meta-analysis and systematic review. *Journal of psychiatric research*, 94, 208-217. - Sonal, A., & Raghavan, V. (2018). Brain derived neurotrophic factor (BDNF) and suicidal behavior: A review of studies from Asian countries. *Asian journal of psychiatry*, 33, 128-132. - Ferrer, A., Labad, J., Salvat-Pujol, N., Barrachina, M., Costas, J., Urretavizcaya, M., ... & Soria, V. (2019). BDNF genetic variants and methylation: effects on cognition in major depressive disorder. *Translational psychiatry*, 9(1), 1-10. d) After Conclusions, but in that section, it should include more data about tendencies observed for remaining suggestion "BDNF is linked to suicidality" e) Check if the repetition of references are required or inadequate (those in supplementary material are in the main references).

## PEER-REVIEW REPORT

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

**Manuscript NO:** 65781

**Title:** BDNF methylation and mRNA expression in brain and blood of completed suicides in Slovenia

**Reviewer's code:** 03197771

**Position:** Editorial Board

**Academic degree:** PhD

**Professional title:** Full Professor

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

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

**Manuscript submission date:** 2021-03-16

**Reviewer chosen by:** Ya-Juan Ma

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**Reviewer performed review:** 2021-04-02 07:57

**Review time:** 5 Days and 15 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 type="checkbox"/> Grade B: Minor language polishing <input checked="" 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 type="checkbox"/> Anonymous <input checked="" type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

## **SPECIFIC COMMENTS TO AUTHORS**

In the case-control study entitled “BDNF methylation and mRNA expression in brain and blood of completed suicides in Slovenia”, the authors explored mRNA levels of different BDNF transcript isoforms and the methylation status of discrete areas of the BDNF gene in an effort to compare two brain areas and blood of suicidal participants with a group of participants who died from cardiac problems. While the value of the analysis is appreciated and the justification by BDNF associations is set by the literature of previous studies, it should be noted that the choice of the control group may determine the findings. What were the control groups used in the cited, previous literature? In addition, and despite the author initial intention, the conclusion reached: “this is the first study that has explored BDNF locus methylation, and the expression of four BDNF transcripts in brain and peripheral blood in the same cohorts” is not considered right. This study could not explore the expression of BDNF transcripts in blood. A justification of the areas of the brain to be studied is missing. In the discussion the authors mention previous studies evaluated other areas of the brain. Perhaps the inclusion of a summary table, or two, of previous studies exploring BDNF methylation and transcripts in the brain indicating the areas explored and control group types evaluated, and blood, could help with a more reasoned interpretation of their findings. Did all blood studies obtain total RNA from whole blood? WBC (white blood cells)? PBMCs (peripheral blood mononuclear cells)? Table 1, only one p-value is shown, but foot legend indicates 2. Table 2, indicate meaning of “t” column. Figure 2, it is not clear what numbers 1-14 refer to. Please indicate nucleotide positions in the reference genome.

The labeling in Supplementary Figure S1. For I2, 5′ of Exon I should be explained. The authors mention that I2 is upstream of exon 1, which do not seem coherent if I2 is the labeling for intron2. Please explain clearly the meaning of this labeling. Table S1 and



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other parts of the paper refer to regions I1, I2, IV, VI etc. The meaning of which should be clearly presented in Tables and Figures (they should be auto-explicative), in addition to its first appearance in text. Review of the English grammar is needed. Remove article “the” before terms like blood in sentences like : “In the blood... “Data obtained from the blood... In addition, the text should be reviewed to avoid repetitions like: “continuum