



## PEER-REVIEW REPORT

**Name of journal:** *World Journal of Experimental Medicine*

**Manuscript NO:** 82822

**Title:** Personalized clinical managements through exploring Circulating Neural Cells and electroencephalography

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

**Peer-review model:** Single blind

**Reviewer's code:** 02482011

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Professor

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

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

**Manuscript submission date:** 2023-01-20

**Reviewer chosen by:** Yu-Lu Chen

**Reviewer accepted review:** 2023-02-17 04:50

**Reviewer performed review:** 2023-02-24 13:14

**Review time:** 7 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 Grade E: Do not publish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>Novelty of this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
<b>Creativity or innovation of this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation



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

Minor revision requirieds



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**Manuscript NO:** 82822

**Title:** Personalized clinical managements through exploring Circulating Neural Cells and electroencephalography

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

**Peer-review model:** Single blind

**Reviewer's code:** 05688164

**Position:** Peer Reviewer

**Academic degree:** BSc, MD, PhD

**Professional title:** Research Fellow

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

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

**Manuscript submission date:** 2023-01-20

**Reviewer chosen by:** Geng-Long Liu

**Reviewer accepted review:** 2023-04-03 07:06

**Reviewer performed review:** 2023-04-12 08:01

**Review time:** 9 Days

<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>Novelty of this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
<b>Creativity or innovation of this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" 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 type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
<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 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**

12 April 2023    Manuscript ID: 82822    Type: Review    Title: ‘Exploring the Circulating Brain Cells and electroencephalography in brain channels: 5xP Personalized Model for Clinical Management of the patients with Alzheimer disease’ by Mehdipour P et al., submitted to Clinical and Translational Research    Dear Authors,    Manuscript ID: Clinical and Translational Research 82822    Mehdipour and colleagues in the present article entitled ‘Exploring the Circulating Brain Cells and electroencephalography in brain channels: 5xP Personalized Model for Clinical Management of the patients with Alzheimer disease’, described how circulating brain cells (CBCs) behavior in the brain cells and in the blood stream could be used as diagnostic tool for early detection of Alzheimer’s disease (AD), and therefore be an available approach for the preventive Medicine and the personalized/target-based therapy. The main strength of this manuscript is that it addresses a timely and needed topic, discussing    the ongoing efforts of scientists to detect and treat AD, which has been a challenge for over a century.

In general, I think the idea of this article is really interesting and the authors’ fascinating observations on this timely topic may be of interest to the readers of Clinical



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and Translational Research. However, some comments, as well as some crucial evidence that should be included to support the author's argumentation, needed to be addressed to improve the quality of the manuscript, its adequacy, and its readability prior to the publication in the present form. My overall opinion is to publish this paper after the authors have carefully considered my suggestions below, in particular reshaping parts of the 'Introduction' and 'Materials and Methods' sections by adding more evidence. Please consider the following comments: 1. I suggest changing the title. In my opinion, in the present form it seems to be too wordy and not enough informative and appropriate. Also, as the reader may still be confused about what the acronyms relate to, I would suggest to not use abbreviations here. 2. Abstract: In my opinion, Authors should consider rephrasing this section. According to the Journal's guidelines, the Abstract should contain most of the following kinds of information in brief form. Please, consider giving a more synthetic overview of the paper's key points: I would suggest rephrasing the results and conclusion to make them clear for readers to understand. That said, I would like the authors to focus on proportionally presenting the background including the objectives, the short summary, and the conclusion without subheadings. The background should include the general background (one to two sentences), the specific background (two to three sentences), and current issue addressed to this study (one sentence), leading to the objectives. The short summary should close with one to two sentences which put the body of manuscript into a more general context. The conclusion should include one sentence describing the main message using such words like "Here we highlight". The conclusion should write the potential and the advance this study has provided in the field and finally a broader perspective (two to three sentences) readily comprehensible to a scientist in any discipline. 3. I would suggest adding a graphical abstract that will visually summarize the main findings of this article. 4.

Keywords: Please list as many keywords as allowed by the journal from Medical



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Subject Headings (MeSH) (<https://meshb.nlm.nih.gov/>) and use as many as possible in the title and in the first two sentences of the abstract. I would suggest adding '(5xP) GPT' as a keyword.

1. In general, I recommend the authors to include more evidence to back their claims, especially in the Introduction of the article, which I believe is currently lacking. Thus, I recommend the authors to focus on deepening the subject of their manuscript, as the bibliography is too concise: nonetheless, in my opinion, less than 50 articles for a research article are too low. Therefore, I suggest the authors to focus their efforts on researching relevant literature: I believe that adding more studies and reviews will help providing better and more accurate background to this study. Furthermore, I would like the authors to clarify the following points in the abstract and the body of manuscript: a) What is the significance of exploring circulating brain cells and electroencephalography in the management of AD? b) How does the 5xP personalized model differ from other approaches to clinical management of AD? c) Are there any promising developments in the early detection and treatment of AD that are discussed in this file?

2. Introduction: I suggest the authors to reorganize the Introduction section, which seems inhomogeneous and dispersive, and specifically, not enough informative as an Introduction should be. I recommend that the authors focus on presenting the following crucial elements of abstract including the introduction, methods, results, and conclusion, with several paragraphs consisting of up to 1000 words, to introduce the main constructs of this study, which should be understood to a reader in any discipline and make persuasive enough to put forward "the main purpose of current research the authors have conducted and the specific purpose the authors has intended by this study. I would like to encourage the authors to present the introduction starting with the general background, proceeding to the specific background, and finally the current issue addressed to this study, leading to the objectives. The Those main structures should be organized in a logical and cohesive manner. For this reason, I believe that a general





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overview about incidence, prevalence and pathogenesis and biochemical hallmarks of AD, for example 'Dissecting Neurological and Neuropsychiatric Diseases: Neurodegeneration and Neuroprotection (<https://doi.org/10.3390/ijms23136991>)', would be very useful. Moreover, I would recommend adding more information on neural substrates of neurodegenerative disorders, specifically on frontal lobe dysfunction, and on related effects on patients' memory and emotional behavior impairments: this information may provide a better understanding of prefrontal cortex's key role and how its disrupted function may contribute to irregular behavioral responses (doi:10.17219/acem/139572; DOI: 10.3390/biomedicines10122999) and therefore to the development of many cognitive dysfunctions (i.e., impaired memory, attention, working memory, problem solving, processing speed, and social cognition) that are common in AD (<https://doi.org/10.3390/biomedicines10123189>; <https://doi.org/10.3389/fnbeh.2022.998714>). Furthermore, I would like the authors to become familiar with the following papers to enrich this manuscript: <https://doi.org/10.3390/biomedicines10050973>; <https://doi.org/10.3390/ijms23094476>; <https://doi.org/10.1186/s41983-022-00455-z>; <https://doi.org/10.3390/biomedicines11020235>; <https://doi.org/10.3390/biomedicines10030544>.

3. Materials and methods: I recommend opening this section with a short introductory paragraph regarding the study design and methodology. Also, I suggest citing more references to ensure the reliability and the integrity of evidence in the study design the authors have built and the methodology the authors applied to this study.

4. Did the authors investigate relationships between the Spectral power ratio and cognitive functions in AD patients? In my opinion, that measure would have provided more information about how the specific ratio pattern could be specifically associated with cognitive dysfunctions in a domain- and diagnosis-specific manner of AD.

5. I would ask the authors to add a



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proper and defined 'Results' section, to adequately state statistical significance of findings. Thus, I believe that this section would benefit from a more detailed and precise rewriting, in order to ensure in-depth understanding of the findings. I recommend that the authors close the results section with a paragraph which put the results into a more general description. 6. Discussion: The authors need to present the independent discussion section with up to 1500 words and to focus on the following essential elements for discussion. Starting with an introductory paragraph, I would like the authors to present the summary of the previous section and to develop discussion on the potential of this study complementing as the extension of the previous work, the implication of the findings of this study, how this study could facilitate future research, the ultimate goal, the challenge, the knowledge and the technology necessary to achieve this goal, the statement about this field in general, and finally the importance of this line of research. 7. In my opinion, the 'Article highlights' section would benefit from some thoughtful as well as in-depth considerations by the authors, that should make their effort to explain the theoretical implication as well as the translational application of their research. 8. I think that a proper and defined 'Conclusions' paragraph would be useful to ultimately summarize key points of the article. In my opinion, this section would benefit from some thoughtful as well as in-depth considerations by the authors and try to explain the theoretical implication as well as the translational application of their research. 9. In according to the previous comment, I would ask the authors to include a proper and defined 'Limitations and future directions' section before the end of the manuscript, in which authors can describe in detail and report all the technical issues brought to the surface. 10. Regarding the Tables and Figures: According to the Journal's guidelines, Authors should provide an explanatory caption for each table within the text. Overall, the manuscript contains ten figures, two tables and 25 references. I believe that this manuscript may carry important value in studying CBCs as





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biomarkers for early detection of AD. I hope that, after these careful revisions, this paper can meet the Journal's high standards for publication. I am available for a new round of revision of this article. I declare no conflict of interest regarding this manuscript. Best regards, Reviewer