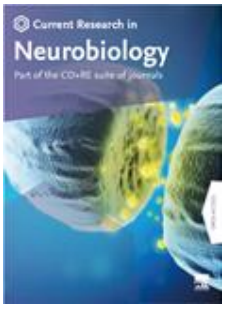
# Peer Review Overview




**Manuscript Title:** The complex relationship between gut microbiota dysregulation and mood disorders: a narrative review

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| Received | Dec 13, 2021 |
| 1st Decision | Feb 07, 2022 |
| 1st Revision Submitted | Apr 09, 2022 |
| Accepted | Jun 01, 2022 |

## 1st Decision letter

**Reference:** CRNEUR-D-21-00073
**Title:** The complex relationship between gut microbiota dysregulation and mood disorders: a narrative review
**Journal:** Current Research in Neurobiology

Dear Alfonso,

Thank you for submitting your manuscript to Current Research in Neurobiology.

I have the reports of two reviewers who recommend reconsideration of your manuscript following major revision. There are issues that need to be addressed with regards to novelty and the quality of the paper

I invite you to resubmit your manuscript after addressing the comments below. Please resubmit your revised manuscript by Apr 08, 2022.

When revising your manuscript, please consider all issues mentioned in the reviewers' comments carefully; outline every change made in response to their comments and provide suitable rebuttals for any comments not addressed. Please note that your revised submission will need to be re-reviewed.

Current Research in Neurobiology values your contribution and I look forward to receiving your revised manuscript.

*CRNEUR* aims to be a unique, community-led journal, as highlighted in the Editorial Introduction. As part of this vision, we will be regularly seeking input from the scientific community and encourage you and your co-authors to take the survey.

Kind regards,

Christopher I. Petkov
Editor in Chief
Current Research in Neurobiology

## Comments from Editors and Reviewers:

**Reviewer #1:**

This manuscript attempts a narrative review of the field of abnormalities of gut microbiota (which the authors refer to as dysbiosis) and affective disorders. Whilst the topic is interesting, there are many weaknesses in the manuscript in its current state. These are detailed below.

1. There have been many reviews written on related topics in the past couple of years, including those listed below. The authors, near the start of their manuscript, need to not these recent related reviews and make it clear as to why their manuscript needs to be published at this point in time.
Examples of related review articles from the last two years alone:
Ortega MA, et al. Gut Microbiota Metabolites in Major Depressive Disorder-Deep Insights into Their Pathophysiological Role and Potential Translational Applications. Metabolites 2022;12(1):50.
Scassellati C, et al. The Complex Molecular Picture of Gut and Oral Microbiota-Brain-Depression System: What We Know and What We Need to Know. Front. Psychiatry. 2021;12:722335.
Misera A, et al. Effect of Psychobiotics on Psychometric Tests and Inflammatory Markers in Major Depressive Disorder: Meta-Analysis of Randomized Controlled Trials with Meta-Regression. Pharmaceuticals (Basel). 2021;14(10):952.
Foster JA, et al. The Relationship Between the Gut Microbiome-Immune System-Brain Axis and Major Depressive Disorder. Front. Neurol. 2021;12:721126.
Kunugi H. Gut Microbiota and Pathophysiology of Depressive Disorder. Ann. Nutr. Metab. 2021;77 Suppl 2:11-20.
Wilkowska A, et al. Gut Microbiota in Depression: A Focus on Ketamine. Front. Behav. Neurosci. 2021;15:693362.
Margolis KG, et al. The Microbiota-Gut-Brain Axis: From Motility to Mood. Gastroenterology. 2021;160(5):1486-1501.
Simpson CA, et al. The gut microbiota in anxiety and depression - A systematic review. Clin. Psychol. Rev. 2021;83:101943.
Tremblay A, et al. The effects of psychobiotics on the microbiota-gut-brain axis in early-life stress and neuropsychiatric disorders. Prog. Neuropsychopharmacol Biol. Psychiatry. 2021;105:110142.
Gubert C, et al. Exercise, diet and stress as modulators of gut microbiota: Implications for neurodegenerative diseases. Neurobiol. Dis. 2020;134:104621.
Needham BD, et al. Gut microbial molecules in behavioural and neurodegenerative conditions. Nat. Rev. Neurosci. 2020;21(12):717-731.

2. The authors use the term 'dysbiosis' in the title in elsewhere. This term has become more controversial in the last couple of years. In the title at least, it could be replace with something like 'gut microbiota dysregulation'.

3. Furthermore, the phrase 'mechanism of correlation' in the title is not appropriate. Mechanisms imply more than just correlations.

4. The article, considering it is covering such a large literature, is relatively brief and not comprehensive. It needs to be better structured, more authoritative and more comprehensive.

5. The figures are minimalist, and not overly informative. The review needs comprehensive figures that address potential mechanism and provide insights based on the large literature in this field.

6. In assessing the large literature, the authors should be critical and make a thoughtful synthesis or integration. They should distinguish between correlation and causation or demonstrated mechanisms.

6. Regarding the lack of comprehensive citations and referencing, the manuscript ignores major neurodegenerative diseases where depression (and other affective disorders) occur as major symptoms, and also show changes in gut microbiota that can be linked to gut dysfunction (including the depression). One of the most striking examples is Huntington's disease. In Huntington's disease, depression is the most common psychiatric feature, and changes in gut microbiota have been demonstrated both preclinically and clinically:
Kong G, et al. Microbiome profiling reveals gut dysbiosis in a transgenic mouse model of Huntington's disease. Neurobiol. Dis. 2018;135:104268.
Wasser CI, et al. Gut dysbiosis in Huntington's disease: associations among gut microbiota, cognitive performance and clinical outcomes. Brain Commun. 2020;2(2):fcaa110.

**Reviewer #2:**

This review addresses the potential contribution of dysbiosis in affective disorders.

Comments:

1. The standard of the English language is poor and needs revision.
2. It would be more appropriate to replace the term "microbiota" by the term "gut microbiota"
3. Line numbers should be added.
4. In the Introduction section, authors state "MDD and BD are two impactful psychiatric diseases with an high incidence". High incidence where?
5. The authors state that "symptoms were induced by administering cytokines to healthy patients (Haroon et al., 2012)". The mentioned referenced is not appropriated.
6. The subsection 3.1 is vague and the reference Haroon et al, 2014 appears 5 times. This subsection should be improved with better selected references. Inflammation in not only related with cytokines. What about nitric oxide? iNOS, COX-2? (Serra et al 2019, doi: 0.1007/s12035-019-1572-8)
7. The concept "microbiota-gut-brain axis" is implicit in all the manuscript, but it is only explained in subsection 3.3. The manuscript should be reorganized.
8. Authors stated that "Lactobacillus, a genus involved in inflammasome activation, was seen to be increased in stressed mice and BD subjects with high IL-6 levels (Painold et al., 2019)". How it can be explained since, generally, Lactobacillus is considered very good for gut health?
9. Although the theme selected for this manuscript constitutes a hot topic these days, this manuscript should be reorganized and better supported with more references.

# 1st Author Response Letter

## Response to comments from Editors and Reviewers:

Dear Prof. Christopher I. Petkov,

Please find enclosed a revised version of the manuscript "The complex relationship between gut microbiota dysregulation and affective disorders: a narrative review", which we previously submitted to Current Research in Neurobiology. Several studies have shown that gut microbiota dysregulation-related neuroinflammation contributes to the development of affective disorders. A better understanding of the molecular pathways involved in the onset of these conditions may allow to identify new therapeutic targets, thus improving the overall management of affective disorders. In our paper, we explain how alterations in gut bacterial ecosystem and subsequent chronic inflammatory processes can influence the onset of mood disorders, as well as their role in the identification of new therapeutic targets. Thank you very much for providing your feedback and for suggesting us to resubmit the manuscript after addressing your comments, which we considered carefully to improve the paper. We report below point by point your comments and we provide our answers.

**Comments from Reviewer 1**

Q1: This manuscript attempts a narrative review of the field of abnormalities of gut microbiota (which the authors refer to as dysbiosis) and affective disorders. Whilst the topic is interesting, there are many weaknesses in the manuscript in its current state. These are detailed below.

A1: We thank the Reviewer for spending time in revising our manuscript and for appreciating the focus of the paper. We took into account all the Reviewer's suggestions and we thus spent efforts in improving the manuscript according to the points raised by the Reviewer. Answers to all the Reviewer's comments are provided below.

Q2: There have been many reviews written on related topics in the past couple of years, including those listed below. The authors, near the start of their manuscript, need to not these recent related reviews and make it clear as to why their manuscript needs to be published at this point in time. Examples of related review articles from the last two years alone: Ortega MA, et al. Gut Microbiota Metabolites in Major Depressive Disorder-Deep Insights into Their Pathophysiological Role and Potential Translational

Applications.Metabolites2022;12(1):50.
Scassellati C, et al. The Complex Molecular Picture of Gut and Oral Microbiota-Brain-Depression System: What We Know and What We Need to Know. Front. Psychiatry. 2021;12:722335.
Misera A, et al. Effect of Psychobiotics on Psychometric Tests and Inflammatory Markers in Major Depressive Disorder: Meta-Analysis of Randomized Controlled Trials with Meta-Regression.Pharmaceuticals(Basel).2021;14(10):952.
Foster JA, et al. The Relationship Between the Gut Microbiome-Immune System-Brain Axis and Major DepressiveDisorder.Front.Neurol.2021;12:721126.
Kunugi H. Gut Microbiota and Pathophysiology of Depressive Disorder. Ann. Nutr. Metab. 2021;77 Suppl 2:11-20.
Wilkowska A, et al. Gut Microbiota in Depression: A Focus on Ketamine. Front. Behav. Neurosci. 2021;15:693362.
Margolis KG, et al. The Microbiota-Gut-Brain Axis: From Motility to Mood. Gastroenterology. 2021;160(5):1486-1501.
Simpson CA, et al. The gut microbiota in anxiety and depression - A systematic review. Clin. Psychol. Rev. 2021;83:101943.
Tremblay A, et al. The effects of psychobiotics on the microbiota-gut-brain axis in early-life stress and neuropsychiatric disorders. Prog. Neuropsychopharmacol Biol. Psychiatry. 2021;105:110142.
Gubert C, et al. Exercise, diet and stress as modulators of gut microbiota: Implications for neurodegenerativediseases.Neurobiol.Dis.2020;134:104621.
Needham BD, et al. Gut microbial molecules in behavioural and neurodegenerative conditions. Nat. Rev. Neurosci. 2020;21(12):717-731.

A2: Thank you for the suggestion. We agree with the Reviewer comment and we further revised previous literature on the topic, which was mainly focused on clear-cut major depressive disorder according to the DSM-5 criteria and did not consider mood symptoms as dimensions that could present in the context of different clinical conditions. Moreover, a huge amount of research took into account neurological diseases and special populations. We thus decided to specify why our review is different from those already existing in the Introduction section (pages 2-3, lines 67-84): “The relationship between gut microbiota and inflammation, as well as their possible link with the development of neuropsychiatric disorders, has interested a lot of research in recent years (Foster et al., 2021; Simpson et al., 2021; Tremblay et al., 2021). The majority of research focusing on psychiatric conditions investigated the role of inflammation in MDD, paying less attention to other diseases classified within

the mood spectrum (Angst & Cassano, 2005). Furthermore, mood symptoms may be present in a number of psychiatric conditions that do not necessarily comply with Diagnostic and Statistical Manual of Mental Disorders 5th edition (DSM-5) criteria for mood disorders, as well as in a number of medical diseases, such as neurodegenerative and inflammatory diseases (Menculini et al., 2021) A better understanding of the molecular pathways involved in the onset of mood symptoms and mood disorders may allow to detect more homogeneous subpopulations of subjects suffering from these conditions. This would help to identify new therapeutic targets in the context of precision medicine, thus improving the overall clinical management of such conditions. On the basis of these premises, this review explores the possible role of gut microbiota dysregulation in the pathophysiology of mood disorders, evaluated as a spectrum, and mood symptoms. Particularly, dysbiosis-related neuroinflammatory mechanisms will be considered. We hypothesize that gut microbiota dysregulation can play a role in the onset of several neuropsychiatric disorders, especially mood disorders."

Q3: The authors use the term 'dysbiosis' in the title in elsewhere. This term has become more controversial in the last couple of years. In the title at least, it could be replace with something like 'gut microbiota dysregulation'.

A3: Thank you for this precious suggestion. We agree about the term "dysbiosis" representing a controversial word during the last years and we thus reworded both in the title and along the text following the Reviewer's recommendation. In addition, we specified what we meant with the term "dysbiosis" in the Introduction (page 2, lines 41-43): "We define dysbiosis as an interruption of the physiological balance of the intestinal microbiota, both in composition and function (Petra et al., 2015; Levyetal.,2017)."

Q4: Furthermore, the phrase 'mechanism of correlation' in the title is not appropriate. Mechanisms imply more than just correlations.

A4: We agree with the Reviewer comment and we thus decided to change the title as follows: "The complex relationship between gut microbiota dysregulation and mood disorders: a narrative review", in order not to advocate causality mechanisms on the bases of the discussed findings.

Q5: The article, considering it is covering such a large literature, is relatively brief and not comprehensive. It needs to be better structured, more authoritative and more comprehensive.

A5: Thank you for the suggestion. Overall, we have tried to make the article more structured, focusing on the coexistence of typical symptoms of mood disorders in different inflammatory clinical conditions and on possible therapeutic implications in the context of precision medicine. Therefore we have added the

subchapter 3.6 Mood symptoms in medical conditions related to gut microbiota dysregulation. Moreover, in the Discussion we emphasized the usefulness of a dimensional approach instead of a categorical one when considering mood disorders in the clinical practice, to provide individualized treatment in the perspective of precision medicine (page 10, lines 321-328): “Moreover, the heterogeneity of mood disorders may partially be ascribed to the symptom-based diagnostic approach operated by the DSM-5. This categorical approach puts different heterogeneous populations into the same category and ignores the different pathophysiological pathways underlying psychiatric symptoms (Sakamoto et al., 2021). To overcome these limitations, a dimensional approach that considers an objective biological measure using body fluids biomarkers, genetic aspects, or multimodal imaging may be useful to detect a more homogeneous subpopulation of subjects suffering from mood disorders or mood symptoms. This approach may allow us to provide individualized treatment in the perspective of precision medicine.”

Q6: The figures are minimalist, and not overly informative. The review needs comprehensive figures that address potential mechanism and provide insights based on the large literature in this field.
A6: Thank you for the suggestion. We agree with the reviewer comment, and we have tried to make the figure 1 more detailed and informative, indeed we decided to summarize relevant information concerning gut microbiota dysregulation in one figure in the subchapter 3.4 Gut microbiota dysregulation and TRP metabolism (Fig.1, page 7).

Q7: In assessing the large literature, the authors should be critical and make a thoughtful synthesis or integration. They should distinguish between correlation and causation or demonstrated mechanisms.
A7: We thank the Reviewer for this precious suggestion. We revised again all the considered literature in depth and we decided to reconsider the terms used in the Discussion, e.g., “correlation”, “mechanisms”, “link”. We subsequently proceeded to an extensive rewording according to the Reviewer’s comment.

Q8: Regarding the lack of comprehensive citations and referencing, the manuscript ignores major neurodegenerative diseases where depression (and other affective disorders) occur as major symptoms, and also show changes in gut microbiota that can be linked to gut dysfunction (including the depression). One of the most striking examples is Huntington's disease. In Huntington's disease, depression is the most common psychiatric feature, and changes in gut microbiota have been demonstrated both preclinically andclinically:
Kong G, et al. Microbiome profiling reveals gut dysbiosis in a transgenic mouse model of Huntington's disease.Neurobiol.Dis.2018;135:104268.

Wasser CI, et al. Gut dysbiosis in Huntington's disease: associations among gut microbiota, cognitive performance and clinical outcomes. Brain Commun. 2020;2(2):fcaa110.

A8: We thank the Reviewer for this precious comment. Based on your suggestions overall we have tried to reorganize the article, focusing on a dimensional perspective to consider affective symptoms that could present in the context of different clinical conditions. Moreover, we added in the subchapter 3.6 Mood symptoms in medical conditions related to gut microbiota dysregulation the topic of affective symptoms in neurodegenerative diseases (pages 8-9, lines 258-273): “In addition, the gut microbiota influences brain function through the gut-brain axis: it regulates the development and function of microglia and astrocytes, which mediate neurophysiological processes including neural development, neurotransmission, neuroinflammation, and blood-brain barrier integrity, also contributing to the pathogenesis and resolution of CNS lesions (Fung et al., 2017). In most of the major neurodegenerative diseases, such as Alzheimer's disease (AD), Parkinson's disease (PD) and Huntington's disease (HD) an alteration in the composition of the gut microbiota has been demonstrated (Wasser et al., 2020). For example, Keshavarzian et al. (2017) showed that proinflammatory Proteobacteria were significantly more abundant in mucosa of PD subjects than controls. On the other side, anti-inflammatory bacteria from the genus Faecalibacterium were significantly more abundant in the mucosa of controls than PD subjects (Keshavarzian et al., 2015). Moreover, differences in bacterial abundance including increased Bacteroidetes, and decreased Bifidobacterium were showed in the microbiome of AD subjects (Vogt et al., 2017). In these neurological conditions, psychiatric, and particularly mood symptoms, occur with a high prevalence (Galts et al., 2019; Menculini et al., 2021). Thus, the occurrence of gut microbiota alterations both in inflammatory and neurodegenerative diseases, as well as in subjects with mood symptoms, could explain the high comorbidity between these medical conditions and psychiatric disorders.”

**Comments from Reviewer 2**

Q1: This review addresses the potential contribution of dysbiosis in affective disorders.

A1: Thank you for spending time reviewing our manuscript. We believe that the topic of gut microbiota dysregulation represents a crucial and innovative issue for clinical practice. We also thank you for your precious suggestions, which we took into account for improving the manuscript standards.

Q2: Comments:

The standard of the English language is poor and needs revision.

A2: We thank the Reviewer for the comment. We revised the text with the aid of a mother tongue colleague in order to improve the English language.

Q3: It would be more appropriate to replace the term "microbiota" by the term "gut microbiota"

A3: Thank you for the suggestion. We agree with the Reviewer's comment and we thus reworded along the text following the Reviewer's recommendation.

Q4: Line numbers should be added.

A4: We added line numbers as requested.

Q5: In the Introduction section, authors state "MDD and BD are two impactful psychiatric diseases with an high incidence". High incidence where?

A5: We thank the reviewer for this suggestion. We thus decided that the term "prevalence" is more appropriate than "incidence" and we added the epidemiological data in the Introduction section (page 2, lines 40-45): "MDD and BD are two impactful psychiatric diseases with an high prevalence worldwide and whose pathophysiology has not been fully understood yet (Malhi & Mann, 2018; Jucevičiute et al., 2019). In particular, BD affects about 1 % of the world's population, but the prevalence rises to 2-4% when considering the whole BD spectrum (Grande et al., 2016). According to the World Health Organization, MDD is a significant cause of disability, and more than 300 million people suffer from this disorder worldwide (De Aguiar Neto & Rosa, 2019)."

Q6: The authors state that "symptoms were induced by administering cytokines to healthy patients (Haroon et al., 2012)". The mentioned referenced is not appropriated.

A6: Thank you for this precious suggestion. We revised again the paper by Haroon et al. and we decided to modify the text, also adding another source to make this concept clearer in the Introduction section (page 2, lines 50-52): "An increase of inflammatory mediators was demonstrated in subjects affected by these conditions (Felger, 2017). Similarly, depressive-like behaviors were induced by administering cytokines to laboratory animals and humans (Raison et al., 2006; Haroon et al., 2012)."

Q7: The subsection 3.1 is vague and the reference Haroon et al, 2014 appears 5 times. This subsection should be improved with better selected references. Inflammation in not only related with cytokines. What about nitric oxide? iNOS, COX-2? (Serra et al 2019, doi: 0.1007/s12035-019-1572-8)

A7: We thank the Reviewer for this precious suggestion. We have tried to improve the subsection 3.1 Gut microbiota dysregulation and inflammatory state following this recommendation (Page 4, lines 131-143): "Additionally, numerous stimuli in the context of gut microbiota dysregulation, e.g., pro-inflammatory cytokines, microbial products, or oxidative stress, can activate the nuclear factor k chain transcription in B cells (NF-kB) pathway (Serra et al., 2019). This cellular signaling pathway is involved in low-grade intestinal inflammation, because activated NF-kB regulates the expression of genes encoding pro-inflammatory cytokines or enzymes, such as cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS) (Surh et al., 2001). Overstimulation of iNOS leads to excessive nitric oxide (NO) production that is involved in neurotoxicity and attenuation of monoamines biosynthesis. It has been hypothesized that dysregulation of the NO signaling pathway may contribute to the onset of mood disorders (Ghasemi, 2019). In particular, levels of nitrate and nitrite were demonstrated to increase in subjects with MDD, and inhibitors of NO signaling exert antidepressant-like effects in various animal models (Ghasemi, 2019). Moreover, some studies indicated that higher plasma levels of NO in MDD subjects were normalized after treatment with some antidepressant drugs (Herken et al., 2007)."

Q8: The concept "microbiota-gut-brain axis" is implicit in all the manuscript, but it is only explained in subsection 3.3. The manuscript should be reorganized.

A8: We thank the Reviewer for this precious suggestion. We thus decided to specify the concept "microbiota-gut-brain-axis" in the Introduction section (page 1, lines 24-29): "In line with the literature, we assume that there is a bidirectional communication between the gut and the brain, which is mediated by gut microbiota. This interaction is also referred to as microbiota-gut-brain-axis (Margolis et al., 2021). Particularly, the gut microbiota influences the central nervous system (CNS) by activating the vagus nerve, by producing microbial antigens that recruit inflammatory cells, and by enteroendocrine signaling from epithelial intestinal cells (Hong-Xing & Yu-Ping, 2016; Cocchi & Gabrielli, 2019)."

Q9: Authors stated that "Lactobacillus, a genus involved in inflammasome activation, was seen to be increased in stressed mice and BD subjects with high IL-6 levels (Painold et al., 2019)". How it can be explained since, generally, Lactobacillus is considered very good for gut health?

A9: We thank the Reviewer for this comment. We revised the considered article because there are some limitations that may influence the results of the study. For example, neither individuals with BD nor controls received a standardized diet and they remained on their usual pharmacotherapy, Moreover, the imbalance between different species is involved in the systemic inflammatory response, while a single genus increased or decreased in number is not a meaningful finding. We thus decided to remove this citation and to specify that Lactobacillus is an anti-inflammatory bacterial genus of gut micriobiota in the subchapter 3.5 "Gut microbiota dysregulation and mood disorders" (page 7, lines 225-233): "Human studies demonstrated the lower abundance of anti-inflammatory bacteria, such as Lactobacillus and Bifidobacterium, in subjects with MDD (Amirkhanzadeh Barandouzi et al., 2020). Moreover, Bifidobacterium, a species that is associated with suppression of inflammatory pathways through inhibition of NF-Kb, was also found to be reduced in stressed mice (Inserra et al., 2018). In animal models, Lactobacillus and Bifidobacterium can decrease the severity of depressive symptoms, also exerting a positive impact on memory, learning and cognition (Serra et al., 2019). On the other side, one study showed that Lactobacillus was seen increased in stressed mice and BD subjects with high IL-6 levels, but findings should be critically revised after considering the study limitations (Painold et al., 2019)."

A10: Although the theme selected for this manuscript constitutes a hot topic these days, this manuscript should be reorganized and better supported with more references.

A10: We thank the Reviewer for appreciating the focus of the paper and we agree on the point that the overall organization of the manuscript could be improved. In consideration of the Reviewer's suggestions, we thus decided to re-evaluate affective symptoms in a dimensional perspective and, overall, we tried to reorganize the article, focusing on the coexistence of typical symptoms of mood disorders in different clinical conditions and on possible therapeutic implications in the context of precision medicine. We also added the subchapter 3.6 "Affective symptoms in medical conditions related to gut microbiota dysregulation" and other references. Moreover, in the Discussion section we decided to emphasize the usefulness of a dimensional approach instead of a categorical one when considering mood disorders in the clinical practice, to provide individualized treatment in the perspective of precision medicine.

# Accept Letter

Dear Prof Tortorella,

Thank you for submitting your manuscript to Current Research in Neurobiology.

I am pleased to inform you that your manuscript has been accepted for publication.

My comments, and any reviewer comments, are below.

Your accepted manuscript will now be transferred to our production department. We will create a proof which you will be asked to check, and you will also be asked to complete a number of online forms required for publication. If we need additional information from you during the production process, we will contact you directly.

We appreciate and value your contribution to Current Research in Neurobiology. We regularly invite authors of recently published manuscript to participate in the peer review process. If you were not already part of the journal's reviewer pool, you have now been added to it. We look forward to your continued participation in our journal, and we hope you will consider us again for future submissions.

*CRNEUR* aims to be a unique, community-led journal, as highlighted in the Editorial Introduction. As part of this vision, we will be regularly seeking input from the scientific community and encourage you and your co-authors to take the survey.

Kind regards,

Christopher I. Petkov
Editor in Chief
Current Research in Neurobiology

Editor and Reviewer comments:

Reviewer 1: The manuscript has been extensively revised and my comments adequately addressed.

Reviewer 2: The paper is now suitable for publication.

*-------- End of Review Comments --------*