Point-by point response to the Reviewers' comments

Reviewer #1 .

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Comments: This paper focuses on neuroinflammatory pathways linking COVID-19 to anxiety and depression. 18% of the introduction resulted plagiarized according to the plagiarismdetector.net application. By the way, all the non-original parts were adequately referred to their sources. The non-original sentences are: - "has been extended to 2030 to include mental health support for individuals affected by the COVID-19 pandemic[17]." - "Chronic stress exposure is a major risk factor for depression and anxiety[21], and the outbreak of COVID-19 is undoubtedly a major cause of stress for people and their communities[22]." - "Depression and anxiety prevalence rates increased over time and doubled compared to estimates before the pandemic[30]." - disorder and anxiety cases, respectively, which substantiates the burden of mental health due to COVID-19 [31]. All the rest of the manuscript resulted as being original. ABSTRACT: generally well written, with a few minor grammatical flows. Line 55 "focusses" -> "focuses". INTRODUCTION: this section should clearly state the main hypothesis and the aims of the study. What do the authors want to prove? What would that add to the current knowledge on the subject? Lines 64-65 "The pandemic has not only impacted the infected patients but also the general population." -> should be rephrased. Line 74 "workload" -> "the workload". Line 78 – 80 "Besides the stress caused in the general population during the ongoing

COVID-19 pandemic, another concern is related to the patients who have been hospitalized due to COVID-19." -> this sentence is wordy; consider rephrasing it. COVID-19 RELATED STRESS AND THE HIGH PREVALENCE OF DEPRESSION AND ANXIETY SYMPTOMS -> Generally well written. Lines 92-93: "The increase in depressive and anxiety symptoms during the COVID-19 pandemic has become a major health concern." -> Literature references should support this statement. Lines 124 – 126 "Another Chinese study conducted in 2020 identified the prevalence of depression/anxiety, or both at 20.4%[26], which was considerably higher than 4% measured in a study conducted in 2019[27]." -> this sentence should be rephrased in a more straightforward form. Line 128 "worry" -> worrying. Line 139 "being more affected" -> being THE MOST affected. Lines 143 – 146 "A systematic review of data reporting the prevalence of depressive and anxiety disorders in 204 countries and territories in 2020 estimated an increase of 27.6% and 25.6% in major depressive disorder and anxiety cases, respectively, which substantiates the burden of mental health due to COVID-19 [31]." -> It is not very intelligible and contains a few grammar mistakes, which should be rewritten. NEUROINFLAMMATION AND PSYCHOLOGICAL MANIFESTATIONS -> Generally well written. Lines 160 -161: "Individuals with depressive symptoms consistently display activation of inflammatory pathways, as revealed by the high serum levels of pro-inflammatory cytokines and acute-phase proteins, as well as an increase in the expression of adhesion molecules and chemokines[34–38]." -> This sentence is hard to follow. Consider rewriting it. NEUROINVASION BY SARS-CoV-2 -> Generally well written. Line 265: "et al" -> et al. Line 272: "literature" -> the literature. CONCLUSION ->

Generally well written. Line 312: "The brain function" -> brain function. Line 315: "Do not affect" -> affect not. GRAPHS AND FIGURES -> the SD should always be shown. GRAPHS AND FIGURES: All good. REFERENCES: All good. REVIEWER'S CONCLUSION: The introduction section should be expanded to state the paper's aim clearly. The discussion could be improved. The English language of the entire manuscript should be revised.

Response: We thank the reviewer for his/her positive feedback and careful text revision. All the requested alterations were done. The introduction was expanded to include the aim of the review. The language of the manuscript was extensively edited and proofread again by Editage.com, a professional English editing service. We made our best to meet the quality requirements of this journal.

Reviewer #2 .

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Comments: This is a thorough review on a relevant topic such as the mechanism of action of COVID 19 on the patients that develop depression. It is quite clear and well-referenced. Ver useful for readers.

Response: We thank the reviewer for his/her positive feedback.