Review of: "Effects of the SARS-CoV-2 Spike protein on in vitro aggregation of alpha synuclein- probable molecular interactions and clinical implications"

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Potential competing interests: No potential competing interests to declare.

The following points should be considered and addressed in the revised version:

1. The abstract and introduction sections are very similar. They should be rewritten according to their definitions.

2. It has been mentioned that some diseases such as Parkinson can be originated from the SARS-CoV-2 and/or vaccination. It is a valuable and important subject for investigation. Interestingly, recently it has been reported that these diseases can be treated by the same method/material, i.e., graphene-based treatment (see, for example, *Biomedicines* 2022, *10*(5), 1000], [ACS Biomaterials Science & Engineering 8 (2021) 54-81], [doi: 10.4103/1673-5374.346486]). This can imply that the same factors can be found in these types of the diseases. This issue should be addressed and discussed in the introduction section of the revised version.

3. In Figure 2, the statistical parameters of the tests such as the number of samples should be given.

4. To avoid the problems mentioned by the authors, designing some recombinant spike proteins have been proposed (see, for example, [doi.org/10.1371/journal.ppat.1008796] and [Chemosphere Volume 306, November 2022, 135578]). This issue should be addressed and discussed in the revised version.

5. The authors talked about the "damage resulting from the central nervous system hypoxia of severe COVID-19" as a right statement. However, this kind of damages can be controlled by various oxygenation methods (see, for example, a review in this regard [ACS Applied Nano Materials 4 (2021) 11386-11412] and an original work [doi.org/10.32794/mr11250069]). Now, whether the following diseases are occurred after these kinds of treatments? Please discuss using suitable supports.

6. Some recent studies regarding the modeling of the interaction of the surface proteins of SARS-CoV-2 virus and the molecules/proteins/chemicals affect it have been published (see, for example, [Biochemical and Biophysical Research <u>Communications Volume 554</u>, 21 May 2021, Pages 94-98], [https://doi.org/10.1002/jmv.26597], [Chemical Biology & Drug Design 100 (2022) 699-721] and [Biophysical Journal <u>Volume 120</u>, Issue 6, 16 March 2021, Pages 1011-1019]). These should be mentioned in the introduction section. Then the novelty of this work should be further highlighted as compared to the previous ones.