

## OPEN PEER REVIEW REPORT 1

**Name of journal:** Neural Regeneration Research

**Manuscript NO:** NRR-D-20-00841

**Title:** Deciphering the role of PGC-1 $\alpha$  in neurological disorders: From mitochondrial dysfunction to synaptic failure

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**Reviewer's country:** USA

### COMMENTS TO AUTHORS

This review is well and carefully written and the summary is concise and systematic. I think more information is needed about PGC-1 $\alpha$  biology and mitochondrial dysregulation.

General remarks:

This review focuses on the potential roles of PGC-1 $\alpha$  in the pathologies of multiple neurodegenerative diseases. Actually, almost all the neurodegenerative diseases share many manifestations including mitochondrial dysfunction, and this topic that PGC-1 $\alpha$  links mitochondrial dysfunction and transcriptional dysregulation in neurodegenerative diseases has been reviewed in some papers before. The authors in this manuscript summarized the changes of PGC-1 $\alpha$  at either mRNA or protein levels in the different neurodegenerative diseases and also discussed the benefits of manipulation of PGC-1 $\alpha$  expression or related signaling pathway (s) in alleviating disease-specific phenotypes. Overall, the writing in this manuscript is concise and the logic is clear and the whole manuscript is easy to follow.

I recommend this manuscript for publication after some adjustments have been taken into account.

- 1) I think the authors should discuss the biology of PGC-1 $\alpha$  from gene to protein in more detail and more systematically, including its history, basic concept, signaling upstream and downstream pathways, biological function, in an independent paragraph, even the authors briefly mentioned some of them in "Introduction". It is better to have one figure describing these points.
- 2) Introduction should be as brief as possible. Some information is better to be put separately after "Introduction" and needs further discussion in detail like the roles of mitochondrial dysfunction in neurodegenerative diseases from a holistic perspective prior to review upon individual disease.
- 3) The relationship between PGC-1 $\alpha$ , PPARGC1A and CNS-specific isoform (s) should be clarified possibly in the "biology" paragraph.
- 4) Although the authors have done well, all the abbreviations should be spelled out upon first appearance throughout the manuscript.
- 5) Some descriptions need to be unified like "HTT" and "Htt".