OPEN PEER REVIEW REPORT 1

Name of journal: Neural Regeneration Research
Manuscript NO: NRR-D-23-00118
Title: Lactate metabolism in neurodegenerative diseases
Reviewer's Name: Kumar Aavula
Reviewer's country: USA

COMMENTS TO AUTHORS

The article 'Lactate metabolism in neurodegenerative diseases' reviews the importance of lactate in neurons and neurodegeneration. Lactate being the major source of energy for neurons, it also functions as signaling molecule, substrate for gluconeogenesis and protein lactylation. Defects in lactose metabolism has been reported in neurodegenerative diseases like Alzheimer's and Parkinson's disease. Growing evidence supports importance of targeting lactose metabolism pathway towards therapeutic development for neuroinflammation associated neurodegenerative diseases. Focused research and knowledge on lactose metabolism in neurons and glia is very much needed.

In this article, authors tried to review lactose metabolism in neurodegeneration. They did a decent job in collecting the information but failed to present it well in the article. Information from different articles was put together with no connection from one another and no concluding remarks at the end. Only two sections 3.2 and 3.3 are presented well, but with section 3.4 arranged between 3.2 and 3.3. It appears like section 3.2 and 3.3 is written by one person and the rest by some other person. So, this article needs a detailed revision and re-writing to narrate the story of lactose metabolism in neurodegeneration (with published evidence) rather than assembling the statements.

In addition, section 1.2, second page lines 20-23: "parts of MCT2 immunoreactivity is located at postsynapse" -- site the source of this Information.

Line 25-48: No connection between statements and no conclusion. significance in neuron and glia?

Section2 line 59: "lactate can work as a signaling molecule for cells and modulate transcription by epigenetic modification, which is called lactylation" -- describe the cell type and cite any neuron or glia related stucies.

Section 2.1: No connection between statements and no conclusion. significance in neuron and glia?

Section 2.2: Histone lysine lactylation
No neuron or glial related study is cited in this topic. Authors didn't comment if this process does even occur in neuron or glia or not.

And in Non Histone lysine lactylation, only one report Hagihara et al 2021 showed some evidence of lactylation on brain and neural activity.

Line 22-45: describe how this is relevant to neuron and glia and in neurodegeneration.

Section 3.1 No connection between statements and no conclusion. The words "However and moreover" are used frequently and in appropriately.