

OPEN PEER REVIEW REPORT 1

Reviewer 1: Tania Cristina Leite de Sampaio e Spohr, Instituto Estadual do Cérebro Paulo Niemeyer, Laboratório de Biomedicina do Cérebro, Brazil.

Comments to the authors:

Strengths: The experimental hypothesis was well founded and the authors made methodological assays to prove the hypothesis raised.

Weaknesses: The authors administrated DFO 30 minutes before injury. And they suggested that DFO as a promising therapeutic approach for SCI. However nobody knows when is going to have a SCI. So for me it is not very logical to administer the DFO 30 minutes before the injury. I think this should be discussed and explored at the discussion section.

The manuscript describes the use of DFO treatment on spinal cord injury (SCI) models. The authors showed that DFO treatment significantly enhanced hind limb function of traumatic SCI rats. The authors also demonstrated that DFO reversed GSH depletion and lipid peroxidation post SCI. Furthermore that DFO protected neurons as well as decreased gliosis. They suggested that targeting ferroptosis is a promising therapeutic approach for SCI.

This original manuscript and is well written, however I have some comments:

- 1) All abbreviations should be described when they appear, i.e. at the abstract section the meaning of GSH, ACSF2 and IREB2 is missing.
- 2) At the page 5, introduction section, first paragraph, the meaning of FDA should be written.
- 3) Page 6, first paragraph, after the sentence "Cell death of motor neurons complete with loss at the epicenter by 4 hours." should be more specific if this happens in rats/mouse or humans.
- 4) The meaning of xCT is missing at the abbreviation section.
- 5) Page 8, at the Results section, the meaning of BBB should be written.
- 6) Page 9, line 23-24, after "in consistent with previous studies that apoptosis occurs at 1-2 days post injury." I think a reference is missing.
- 7) Page 13, the meaning of GFAP should be written at the text.
- 8) Page 15, line 20 after "As iron chelation could also rescue ferroptosis in vitro in cancer cells,..." I think a reference is missing.
- 9) Page 15, line 31, after "is involved in intracellular iron storage." I think a reference is missing.
- 10) Page 15, line 51, after "but only few studies have explored the effects of ferroptosis on acute injury of CNS." I think a reference is missing.
- 11) Page 16, line 20, after "as well as Lipid ROS accumulation." I think a reference is missing.
- 12) Page 19, line 9, after "could be rescued by Vitamin E." I think a reference is missing.
- 13) The authors administrated DFO 30 minutes before injury. And they suggested that DFO as a promising therapeutic approach for SCI. However nobody knows when is going to have a SCI. So for me it is not very logical to administer the DFO 30 minutes before the injury. Maybe it should have been 30 minutes after the injury. So I think the authors should discuss this a bit at the Discussion section. Why they the administrated the DFO 30 minutes before and not after.
- 14) The scale bar is missing at figure 6. Furthermore the resolution is no so good and therefore it is difficult to see the staining.
- 15) The scale bar is missing at figure 7.
- 16) The schematic drawing should also have a legend.