Reviewer's report

Title: Protective effects of cardiotonic pills on damage induced in the white matter and hippocampus by chronic cerebral hypoperfusion

Version: 2 Date: 15 August 2013

Reviewer: zhong-xiang Yao

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Major Compulsory Revisions

The authors want to examine whether CP treatments ameliorate the brain damage induced by chronic cerebral hypoperfusion. By using histochemistry and western blotting, it is found that CP may ameliorate white matter and hippocampal damage induced via chronic cerebral hypoperfusion by attenuating the induction of white matter lesions and neuroinflammatory processes; furthermore, the suppression by CP upon the inflammatory reaction might be involved in MAPK signaling. They suggested that CP may be a potential candidate for the prevention and treatment of AD and VaD.

The major revisions:
1. Please explain the relationship among the MAPK signals and inflammatory mediators at the whole hippocampal levels, and oligodendrocytes or microglia at cell levels.
2. Why do you choose this dose of CP and this period of CP administration?
3. The title should be more accurate on the effects of CP.

The minor revisions:
1. In abstract, methods line 1: “Wister rat” should be “Wistar rat”.
2. In abstract, conclusion line 2-3: “a trait that suggests therapeutic potential for the prevention of vascular dementia” is not suitable.
3. In background, paragraph 4 line 3-5: “CP treatments restored the reduced expression levels of myelin basic protein (MBP) and reduced microglial activation in the white matter” is confused.
4. In methods, “Animal surgery and drug administration” paragraph 1 line 1: “using a mixture of 5% isoflurane and oxygen” is confused.
5. In methods, “Animal surgery and drug administration” paragraph 1 line 6: “During hypoperfusion, approximately 4% of the rats”, the 4% should give an accurate number too.
6. In methods, “Animal surgery and drug administration” paragraph 1 line 9: the accurate number of the “excluded” rat.
7. In methods, “Animal surgery and drug administration” paragraph 2 line 7: “until the end of the experiment”, the accurate time of the experiment.
8. in methods,” Animal surgery and drug administration” paragraph 2 line 7:” During drug administration, 8 rats were lost”, which group of these 8 rats belong to?

9. in methods,” Western blot analysis” paragraph 1 line 1: “on day 63” should give the beginning time.

10. in methods,” Western blot analysis” paragraph 1 line 2: “Tissue homogenates” will tell us the accurate region of sample.

11. in methods,” immunohistology”, the subtitle: should be “immunohistochemistry”.

12.in results, “CP treatment increased chronic BCCAo-induced MBP reduction in the white matter and hippocampus ”, paragraph 1 line 9: “including the corpus callosum, fimbria, fornix, and hippocampus” is easier to be confused.

13. in results,” CP inhibited chronic BCCAo-induced microglial activation in the white matter and hippocampus” paragraph 1 line 10: “callosum, fimbria, fimbria, and hippocampal subregions”, there are two “fimbria”.

14.in Figure legends, Figure 1 line 1: “the chronic BCCAo-induced”, sometimes it uses the “chronic”, sometimes not(such as in Figure 2 line 1).

15. in Figure legends, Figure 2 line 3-4: “including the corpus callosum, fimbria, optic tracts, and the hippocampal subregions” is easier to be confused.

16. in Figure legends, Figure 2 line 6: lacking of the “C,D,F,G,H” in the legend.

17.in Figure 1, Fornix at BCCAo+Vehicle, the picture is not clear, please change it.

Level of interest: An article of limited interest

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests.