Author's response to reviews

Title: Electroacupuncture at different frequencies (5Hz and 25Hz) ameliorates cerebral ischemia-reperfusion injury in rats: possible involvement of p38 MAPK-mediated anti-apoptotic signaling pathways

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Author's response to reviews:

Dear Dr. Rowles:

Thank you for your dealing with the manuscript entitled “Electroacupuncture at different frequencies (5Hz and 25Hz) ameliorates cerebral ischemia-reperfusion injury in rats: possible involvement of p38 MAPK-mediated anti-apoptotic signaling pathways”, coded as MS: 1767418987155096. The manuscript has been revised and compiled as the reviewers’ suggestions. Our point-by-point reply to the reviewers’ comments is described as follows:

Reviewer: Jakob Troppmair

We have revised the manuscript according to the review’s comments.

1. We have altered the title of the manuscript, and the title of the manuscript has been changed to “Electroacupuncture at different frequencies (5Hz and 25Hz) ameliorates cerebral ischemia-reperfusion injury in rats: possible involvement of p38 MAPK-mediated anti-apoptotic signaling pathways”.

2. We have recomposed the Abstract section from lines 18 p.2 to lines 4 p.3. The revised description is “Conclusion: Both EA-5Hz and EA-25Hz effectively downregulate reactive astrocytosis to provide neuroprotection against cerebral infarction, most likely by activating the p38 MAPK/CREB signaling pathway. The modulating effects of EA-5Hz and EA-25Hz on Bax-mediated apoptosis are possibly due to the activation of p38 MAPK/CREB/Bcl-xL and p38 MAPK/CREB/Bcl-2 signaling pathways, respectively, and eventually contribute to the prevention of Smac/DIABLO translocation and subsequent restoration of XIAP-mediated suppression of caspase-3 in the cortical periinfarct area 7 d after reperfusion.”

3. We have also recomposed the Discussion section from line 1 p.21 to lines 5 p.21 and from lines 14 p.22 to lines 19 p.22. The revised descriptions are “Based on previous reports and our results, we propose that EA-5Hz and EA-25 Hz both
provide neuroprotection against astrocyte-mediated toxicity, most likely by activating p38 MAPK signaling, and that their neuroprotective effects are possibly due to the activation of p38 MAPK/CREB, but not p38 MAPK/HSP70, signaling in the ischemic cortical penumbra 7 d after reperfusion.” and “Considering these and previous findings, we suggest that both EA-5Hz and EA-25Hz exert neuroprotective effects against Bax-mediated apoptosis, possibly due to the activation of p38 MAPK/CREB signaling, and that the downregulating effects of EA-5Hz and EA-25Hz on the insertion of Bax into mitochondria can be attributed to increased mitochondrial Bcl-xL/Bax and Bcl-2/Bax ratios, respectively, but not suppressed p53 signaling, in the cortical periinfarct area 7 d after reperfusion.”

4. In additional, we have recomposed the Conclusions section from lines 19 p.24 to lines 5 p.25 and the revised description is “Overall, our results suggest that EA-5Hz and EA-25Hz both effectively downregulate reactive astrocytosis to provide neuroprotection against cerebral infarction, most likely by activating p38 MAPK/CREB signaling. The modulating effects of EA-5Hz and EA-25Hz on Bax-mediated apoptosis are possibly due to the activation of p38 MAPK/CREB/Bcl-xL and p38 MAPK/CREB/Bcl-2 signaling, respectively, thereby preventing Smac/DIABLO translocation and restoring XIAP-mediated caspase-3 inhibition in the ischemic cortical penumbra 7 d after reperfusion.

Please handle our manuscript at your convenience. Thank you for your kindly help.

Sincerely yours,

Chin-Yi Cheng