Author’s response to reviews

Title: Neuroprotective effects of amiodarone in a mouse model of ischemic stroke

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Author’s response to reviews:

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Lingling Tian
Editor
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Guangde Tu
Editor
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Dear Editors,

Title: Neuroprotective effects of amiodarone in a mouse model of ischemic stroke

Manuscript Number: BANE-D-17-00219

Thank you very much for the opportunity to revise and resubmit our manuscript for publication in BMC Anesthesiology. We appreciate your careful reading and constructive suggestions.

We have revised the manuscript according to the reviewers’ and your comments.
We hope that our revised manuscript will be accepted for publication in BMC Anesthesiology and look forward to hearing from you.

Yours sincerely,

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Answers to the editor and reviewer comments:

Editor Comments:

1 In order to adhere to submission guideline, please rename the section heading 'Ethics approval' to 'Ethics approval and consent to participate'.

We have changed the name of the section heading to 'Ethics approval and consent to participate'.

2 Please provide a section 'Consent for publication' in declarations and state Not Applicable in this section. Even 'Consent for publication' is not applicable for your manuscript, this section must be present.

We have added the section and stated Not applicable.

3 Competing interests

It is stated that 'None of the authors has any potential financial conflict of interest to disclose related to the manuscript.' Both financial and non-financial conflict of interests must be declared, so you may want to state None if you have nothing to declare in this section.

We changed our answer to “None” in this section.

4 Upon resubmission, Please remove any tracked changes or highlighting and include only a single clean copy of the manuscript. Please ensure the document is in the final form for publication; please upload only files that are to be published. If you wish to respond to these revision requests, please insert the information in to the designated input box only.
We removed the highlighting from the revised manuscript.

Reviewer comments:

W. Scott Jellish (Reviewer 1):

This is the first revision of the manuscript entitled, "Neuroprotective effects of amiodarone in a mouse model of ischemic stroke". Briefly, this study assesses the effect of a dose of amiodarone 50 mg/kg on mice that were given a focal cerebral insult by occlusion of the left middle cerebral artery. Amiodarone was given either one hour prior to MCA occlusion or immediately after MCA occlusion in another group. Behavioral testing was assessed 48 hours after MCAO and compared between groups and control. Brains were harvested and infarct volume compared between groups. They found heart rates were lower in the animals that received amiodarone compared to control. Mice that received amiodarone one hour before MCAO had reduced infarct volume compared to saline control or post MCAO treatment. The pretreated rats also had better behavioral testing compared to post treatment or control. The authors conclude that amiodarone pretreatment attenuates ischemic brain injury and improves functional outcomes.

1. The authors have added information to better describe the functionality and what neurologic function the body asymmetry and swing rates assess.

2. They added another experimental group using veratrine, a Na+ channel opener which demonstrated that amiodarone's neuroprotective effect may be due to blockade of Na+ channels. The possible reason post MCAO treatment did not provide neuroprotection is that the amiodarone did not reach the ischemic site due to permanent occlusion of the MCA and no reperfusion was produced. They also addressed other minor critiques by the second reviewer.

3. There are two minor grammatical changes that need to be addressed. These are minor changes that can be addressed by the editor.

   a. Discussion, second page, line 10: place "the" before "pharmacological"

   b. Discussion, fourth page, line 35: place "a" before "neuroprotective"

   c. The authors have done a good job at addressing the queries by the reviewers. The addition of the group with added veratrine and the other group with added isoproterenol demonstrates the mechanism of this neuroprotection and further strengthens the study.

Thank you for your careful review and constructive comments.

We have corrected the grammatical errors.

Creed Stary (Reviewer 2):
The Authors have substantially improved the manuscript with the inclusion of additional mechanistic experiments. There remain only minor English language errors.

Thank you for reviewing our manuscript and the supportive comments. We have corrected the grammatical errors and revised the manuscript according to the editor and the other reviewer, which we believe improved the manuscript.