Author's response to reviews

Title: Hydrogen sulfide and mild hypothermia can selectively activate synaptic NMDARs and trigger the CREB signaling pathway

Authors:

Hai-bin DAI (Dai_hai_bin1@163.com)
Yi-min HU (Hu_yi_min@163.com)
Li-dong ZHANG (Li_dong_zhang@163.com)
Xiao-lei MIAO (Miao_Xiao_lei@163.com)
Si-hai ZHU (Zhu_si_hai@163.com)
Man-lin DUAN (Duan_man_lin@163.com)
Wei-yan LI (lee_wei_yan@163.com)

Version: 2
Date: 15 January 2015

Author's response to reviews: see over
Dear Editor:

We would like to submit the enclosed manuscript entitled "Hydrogen sulfide and mild hypothermia can selectively activate synaptic NMDARs and trigger the CREB signaling pathway", which we wish to be considered as an original article for publication in BMC Anesthesiology. This manuscript substantiated the theory that hydrogen sulfide selectively activated synaptic NR2A subunits, which appeared to further mediate downstream pro-survival signaling pathways. Meanwhile, mild hypothermia possibly functioned to activate the CREB pathway by inhibiting the overexpression of extra synaptic NR2B.

N-methyl-D-aspartate (NMDA) receptor is regarded as a critical factor in neuronal damage following ischemia-reperfusion insult such as stroke or brain trauma. The activation of NMDARs at synaptic locations promotes neuronal survival, whereas activation of NMDARs at extrasynaptic locations will promote neuronal death. Hydrogen sulfide, an endogenous gas-signaling molecule, has an important role in protecting central nervous systems. Mild hypothermia (30~33oC) has been wildly recognized to have a significant protective effect in the treatment of traumatic brain injury. In this study, we established the rat hippocampus following global cerebral ischemia-reperfusion model to further investigate the synergistic effect of brain recovery by both exogenous administration of the H2S donor compound, NaHS, and mild hypothermia. Moreover, during brain recovery, synaptic NMDARs associated with the CREB and PI3K-Akt
signaling pathway have been discovered in this study to be a key pro-survival mechanism.

Our new findings provide the evidence that potential value of application of NaHS and mild hypothermia in treatment of ischemia-reperfusion damages. This study may produce certain data available for health care decision-making.

No part of manuscript has been submitted or accepted for publication elsewhere. All authors approve the submitted version of this manuscript and have contributed significantly to the work.

We hope that you will share our enthusiasm for our findings and consider our manuscript for the journal. We would like to thank you in advance for your consideration and look forward to your favorable decision.

Sincerely,

**Corresponding author:**

LI Wei-yan (MD)
Department of Anesthesiology, Jinling Hospital, School of Medicine, Nanjing University No. 305 East Zhongshan Road, Nanjing, PR China, 210002,

Email: lee_wei_yan@163.com
TEL: +86-025-80860114
FAX: +86-025-84805383

Potential reviewers

1. Yong G. Peng
University of Florida College of Medicine, America
Email: ypeng@anest.ufl.edu

2. Deng Xiaoming
Shanghai Changhai Hospital
Email: xmdeng@anesthesia.org.cn

3. Xu Lixian
School of Stomatology, the Fourth Military Medical University,
Email: xlx116@fmmu.edu.cn