19<sup>th</sup> November, 2018

Ruo-Yu Ma

Science Editor,

World Journal of Gastroenterology

Dear Dr. Ma

Thank you very much for your further comments on our manuscript entitled "Effects of

positive acceleration (+Gz stress) on liver enzymes, energy metabolism, and liver

histology in rats" (Manuscript NO: 43250). According to the constructive comments, we

have revised the manuscript by incorporating additional information (highlighted in yellow)

in the text.

We are grateful for the opportunity to address the reviewers' comments, and hope that

the revision meets the requirements of World Journal of Gastroenterology.

Sincerely yours,

Hongyi Zhang, MD, PhD

Corresponding author

E-mail: qhcgzhy@163.com

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## Response to the Reviewers' Comments

Reviewer: 1

No further comments.

Reviewer: 2

No further comments.

Reviewer: 3

No further comments.

## Reviewer: 4

1. The portal venous flow was significantly decrease after +Gz stress. However the author described that the portal vein diameter did not changed. Why did this phenomenon occur? Because, it is too strange phenomenon, the author should discuss in this manuscript.

We appreciate this suggestion very much. We have discuss the cause of this phenomenon in the manuscript. The specific reason have not yet been entirely clear, but it was assumed to be relate with hydrostatic pressure, velocity and capacity of the portal vein.

2. The transaminases in +Gz groups were increased just after +Gz stress, but these were return to normal levels on next day. On the other hands, MDA levels were continue to increase until 24 hr after Gz stress. Why did the oxidative stress persist, but the liver function recovered?

It was a very good question. Oxidative stress was considered an important factor in liver injury and a remarkably positive correlation existed. Our results showed that their variable trends had no great difference and the recovery extent of oxidative stress lag behind the liver function. We'll do the next experiment to probe into this reason.

3. The author described the hepatic ischemia/reperfusion injury were occur during +Gz stress. However hepatic transaminase is not so increased after 5-10min I/R injury in other models. Moreover, some previous papers reported that short duration of hepatic ischemia can attenuate liver I/R injury in human and animal models. Why severe liver injury was occurred after short +Gz stress (I/R injury)?

During flight, direct action and stress response caused by repeated +Gz exposure may cause liver I/R injury. There are two main reason for short +Gz stress (I/R injury): one is redistribution of blood, and the other is displacement deformation of liver.