

## **Response to comments**

**Reviewer's code: 02728252**

**Comments:** It is a comprehensive narrative review about neural stem cell transplantation therapy for brain ischemic stroke. It is an interesting review, well-constructed with an easy and simple language to understand for the reader.

**Response:** Thank you very much for your support and approve of our manuscript. We believe that this paper will be of interest to the readership.

**Reviewer's code: 01851506**

**Comments:** In this paper, the authors summarized the current methods and their limitation to treat the brain ischemic stroke. The methods include use of neural stem cells (NSCs), combinatorial use of NSCs with cytokines, and exome from NSCs. Whilst the subject is intriguing, in general, the text was not enough elaborated so that the readers outside the field could readily follow and understand the contents. In particular, the reviewer does not understand why the authors put the exome story in the “perspective” section. Given that exome is potential tool for the brain ischemic stroke treatment, this should constitute a part of 4 (Optimizing the therapeutic efficacy of NSC transplantation). In addition to the above criteria, the reviewer is afraid that the font size in the figures is too small.

**Response:** Thanks for your suggestions, the optimized therapeutic strategies (such as gene overexpression, preconditioning or co-transplantation with factors, etc.) of NSC transplantation have been explored by many preclinical studies. However, there are still some limitations and potential side effects, such as potential allogeneic rejection, risk of tumorigenicity, and lower grafting efficiency of transplanted cells etc. Thus, exosomes derived from NSCs as a new therapeutic strategy based on cell-free treatment, will play more important role on treating ischemic stroke in the future. In addition, we have improved the font size of the Figures in the revised version.