**Reviewers' comments:**  
  
Please note that the reviewers raised some significant concerns regarding your method and your manuscript. Please thoroughly address each concern by revising the manuscript or addressing the comment in your rebuttal letter.  
  
  
Reviewer #1:  
  
The methods article presented by Zhao et al is a concise and well-written work regarding the induction of sub-acute cerebral microhemorrhages (CMHs) in rats by way of LPS injection. Although other methods to induce CMHs are established in other animal models, there is clear justification for creating this model in rats. Please cite previous attempts to induce cerebral microhemorrhages in rats with a micro collagenase injection (G McAuley, M Schrag, S Barnes, A Obenaus, A Dickson, W Kirsch. In vivo iron quantification in collagenase‐induced microbleeds in rat brain. Magnetic resonance in medicine 67 (3), 711-717); the model proposed by the Zhao and colleagues in my view is an improvement over the technique previously employed. The article elaborates on methods to detect CMHs in rats and the inclusion of SWI images is a particular strength of the current study as histological techniques can easily overlook areas of microhemorrhage. A complete table of all materials and equipment was references in the paper, but appears to be missing -- this would be useful for future investigators utilizing this method and should be added prior to publication. It might also be useful to also include how controls were obtained (i.e. were the negative control rats only treated with vehicle?). This group did a great job demonstrating the efficacy of the methods used as highlighted in the figures provided but it might be advisable that the figures be annotated more definitively so readers can verify results without having to make assumptions. Still, this group has proven their methodology to be reasonable and effective.  
  
  
  
  
Reviewer #2:  
  
Major Concerns:  
I think the manuscript is sound, but it requires extensive editing for language. I believe it will need re-review by the authors after editing is completed, to assure fidelity. After the authors have check it, I would like to reread it.  
  
  
  
  
Reviewer #3:  
  
Manuscript Summary:  
The manuscript presented by Zhao and colleagues titled "Establishment and detection of sub-acute micro-haemorrhages model in rats induced by lipopolysaccharide injection", outlines a method of the production and detection of cerebral micro-haemorrhages (CMH) in adult Sprague-Dawley rats, as a result of multiple intraperitoneal injections of LPS.  
  
Major Concerns:  
This is a quick and relatively cheap method of producing cerebral micro-haemorrhages. What is not clear from the manuscript as it currently stands is what the normal micro-haemorrhage burden is in each animal or the reproducibility of the method. The authors acknowledge that this model does not replicate the clinical distribution of cerebral micro-haemorrhages; an apparently common reality in models of inflammation-induced CMH. Given the lack of clinical relevance, and the abundance of other models, it is not clear whether this model adds anything to the field, despite the easy and cost-affordability it offers experimenters. A more detailed introduction/discussion of the other methods in the field and the nature of the CMHs produced in the model might help.  
  
Minor Concerns:  
For a methods paper, the details in the protocol are quite superficial. For instance, the serotype of LPS is not given, nor the batch number. However, there is substantial awareness in the field that the response of animals to LPS is highly dependent on serotype, batch and storage.  
More minor details that are missing or unclear include:  
i) Is mounting media used for cryosectioning, if so, which one?  
ii) The manuscript states that action 4.2.1 will only be performed for gross observation of CMHs, but surely this is a standard element of any perfusion fixation protocol?  
iii) What does "the environmental cleanliness need to be maintained" actually mean in reality, in action 3.3? Likewise, what is the "certain but definite systemic inflammation response" that occurs in this model. Given the potential 10% death rate, should researchers be monitoring animals for signs of distress? How frequently? For what features? Is it necessary to have a humane end-point to these experiments?  
iv) What stage of anaesthesia should be reached in section 4.1.1 before section 4.1.2 can be started?  
v) The MRI method appears to be out of sequence. Is the information provided really sufficient for the method to be successfully reproduced by other researchers?  
vi) Is perfusion fixation, without further fixation by immersion, sufficient for good tissue preservation?  
  
The whole manuscript needs extensive editing by a native English speaker.