Reviewer's report

Title: The Effects of Stress on Myocardial Apoptosis in myocardial infarction

Version: 1 Date: 7 June 2012

Reviewer: Ove Wiborg

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Major Compulsory Revision

Although this is an interesting preclinical study on issues relating to comorbidity of MI and MDD the amount of data are too sparse to allow essential conclusions, additionally there are some concerns on the applied methodologies and study design.

The design is unclear. Does Post-MI depression mean: MI followed by CMS (MI + CMS)? The reverse order CMS + MI would also have been interesting. Generally depression should be replaced by CMS or anhedonic-like. Sucrose pref. is a variable parameter and should rather be measured weekly than just at endpoint. Was suc. pref. measured after MI and thus before CMS? Did only 7 out of 20 rats become anhedonic? Were the rest resilient to stress, like reported by others? In case so they should have been included.

In general heart performance should have been analyzed more detailed

Authors mentioned in the methods that they have made ECG recordings - it would have been nice to see be nice a fig with representative traces before and after MI. It is important because there is not many groups which are doing this.

The global problem of the manuscript that it lacks "n" for experiments, graphs, and statistics in the text.

It is important to see / to measure the cardiac performance in different groups before killing the animals. It can be done directly by the same anesthesia before they take the heart out. All mental state changes could be just due to fall in cardiac output, poor brain (and the rest of the body) perfusion etc.

Results, pg. 11, Infarct size. I cannot understand how 65% MI in total became 43% and 46% in each group separately.

Results, pg. 11, Bax:Bcl2 ratio. It is not clear from the text whether the authors are talking about mRNA or protein - they have to specify this and address each result separately, even if they are similar. In fact the method for mRNA recordings should be replaced by real-time recordings which is much more reliable.

This is very intriguing with Bax:Bcl2 ratio, especially with respect to the most significant increase in this ratio in MI+CMS group. Is it consequence of something general in this model of depression? To test this the authors could measure Bax:Bcl2 ratio in different groups, or in another region which have not been exposed to hypoxia. Would there be a difference between the depression
and the control here?

Authors have not found any difference in Caspase-3. But this is not the only caspase which can be involved in apoptosis. What about others? They comment this possibility in the discussion but they could do a bit more about it. F.ex. they could look in the literature whether other caspases expresses in the heart, or even to do their own test. If they could find other caspase they need to see whether it is affected by MI and depression.

1. They need identify the type of Stress in the title. This is especially important because in the "cardiovascular world" stress has, first of all, absolutely another (mechanic) meaning.
2. They need to identify the pharmacological origin of venlafaxine (that this is SNRI)
3. All abbreviation in the abstract (TTC) need to be explained.
4. I think that the conclusion of the Abstract is too generalized and has to describe the specific findings in this study.
5. What is the percentage of rats that survive after MI induction procedure?
6. Pg.10, Statistical analysis, line 2. ".to examine the difference between ."
7. Results, pg. 11, Infarct size, 1st line. Too many labels of %.
8. Pg. 6 line 7-8: The model of dep. replace by The readout on depression status..
9. Pg. 8 line5: rat model replace by readout

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.