Reviewer’s report

Title: Chronic administration of parecoxib exerts anxiolytic-like and memory enhancing effects and modulates synaptophysin expression in mice

Version: 0 Date: 10 May 2017

Reviewer: Martin Kaczocha

Reviewer’s report:

This is an interesting manuscript describing anxiolytic and memory enhancing effects of the COX inhibitor parecoxib. The study is well designed and the conclusions are appropriately drawn from the data. I have several comments and suggestions to improve the manuscript.

1. The authors need to quantify the brain (e.g., hippocampus and amygdala) levels of prostaglandin E2 which is a downstream product of COX2 activity. This is important because the 10 mg/kg dose produced profound enhancement of memory effects while the lower doses did not. Could this be due to incomplete COX2 inhibition by the lower doses of parecoxib? This would provide a mechanistic link to the discrepancy between the high dose and lower doses of parecoxib.

2. Have the authors examined SYP expression after lower doses of parecoxib? Is the effect of parecoxib upon SYP expression only exerted by the highest dose used? This should be included in the manuscript.

3. Although likely beyond the scope of the manuscript, the authors may wish to run an additional cohort of mice that are administered parecoxib in the presence of a cannabinoid receptor 1 antagonist. COX2 inhibitors have been suggested to produce anxiolytic effects through enhancement of endocannabinoid signaling and the inclusion of this group of animals would provide insights into whether chronic parecoxib administration produces its effects through modulation of endocannabinoids.

Minor points

1. On page 11, it appears that different fonts are used.

2. In the methods, the catalog numbers (and ideally RRIDs) of the antibodies should be provided.

Are the methods appropriate and well described? If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

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I am able to assess the statistics

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