Reviewer's report

Title: Disruption of the endothelin A receptor in the nephron causes mild fluid volume expansion

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Reviewer: Ivana Vaneckova

Reviewer's report:

This study evaluates the effect of the genetic disruption of endothelin A receptor on blood pressure and salt handling in mice with doxycycline-induced nephron specific deletion of ETA receptor. The authors conclude that this genetic manipulation leads to a mild fluid retention suggesting a minor role of nephron ETA receptors in sodium handling under physiological conditions.

Major comments:

The authors should discuss the changes in body weight and decreasing hematocrit in view of unchanged extracellular fluid and total body water under high salt intake. What was the percentage change of body weight during the experiment?

Minor comments:

1. Were male or female used in the experiments? There could be different effects on male and female on sodium handling as has been previously shown in rats. Discussion to this topic should be added.

2. In the statistical analysis, it is stated that mean percent of control were analyzed, however also absolute values (Fig 5 and 6) were used in the study-please correct this.

3. Figure 4-the description of experimental schedule is different in figure and methods section. In the figure, it should be better to number the days following doxycycline treatment sequentially, i.e. 21, 22 etc in order to highligh that it is the continuation of the experiment.

4. Fig 6-the authors should explain why different time schedule (7+7 days instead of 3+7) for the experiments with body volume status were used.

5. Fig.6-the explanation of statistical significances is missing. SI units use kilograms (kg) for weight.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

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

'I declare that I have no competing interests'