Reviewer's report

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

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Reviewer: Olaf Grisk

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The present study investigated the role of renal epithelial ETA receptors for sodium and fluid homeostasis using a tissue-specific inducible knock out model. The study shows that renal epithelial ETA-R knock out does not lead to increased sodium sensitivity of arterial pressure but causes modest volume retention under conditions of high NaCl intake based on body weight, impedance and hematocrit measurements.

Two minor essential revisions
The authors conclude that ETA-R disruption in the nephron causes mild Na+ retention. The difficulty to detect subtle differences in Na+ and water balance by metabolism cage studies in mice is acknowledged. The metabolism cage protocol did not allow detecting transient changes in sodium and water balance in response to the switch from normal to high NaCl diet. Was water and sodium intake measured for calculation of respective balances? If no direct evidence for increased Na+ retention in response to renal epithelial ETA-R knockout can provided so far, it is suggested to substitute Na+ retention by volume retention in the conclusion.

The legend of Fig. 6 should indicate what statistically significant difference the asterisks indicate to facilitate reading.

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.