Reviewer's report

Title: Effect of Volume Expansion with Hypertonic- and Isotonic Saline and Isotonic Glucose on Sodium and Water Transport in the Principal Cells in the Kidney.

Version: 1 Date: 3 July 2013

Reviewer: Eric Féraille

Reviewer's report:

In this manuscript, Jensen et al. studied the effect of acute plasma volume expansion using isotonic (0.9% NaCl), hypetonic 3% NaCl) or hypotonic (5% glucose) solute infusion on urinary water and Na excretion as well as urinary AQP2 and gamma-ENaC excretion in healthy humans. This is an interesting and carefully performed study. The manuscript is well written. However results are mostly presented in non-reader friendly tables. I would have a few comments on this study.

1 - It should be interesting to calculate the fraction of infused water and solute that has been excreted after 240 min. In addition, measurement of plasma albumin concentration may provide some information on plasma volume. These informations can be useful for the discussion of experimental results.

2 - The authors should also provide values of urinary potassium excretion that may argue against or for a major role of ENaC-mediated Na transport in the observed changes. If ENaC is primarily involved, one could expect opposite changes in urinary K excretion.

3 - The possible effects of various experimental conditions on the thiazide-sensitive NaCl cotransporter in distal tubule should be discussed

4 - Measurement of AVP concentration may not be sensitive enough to detect a small decrease in plasma AVP. This might be discussed. In addition the role of recently discovered hormone apelin should be discussed

5 - In addition to AVP increased extracellular tonicity can increase apical cell surface expression of AQP2 in collecting duct principal cells (Hasler et al. J Biol Chem. 2008, 283: 26643-61). This should be discussed.

6 - The first part of the discussion should be deleted since it recapitulates the results

7 - Abbreviations should be given after the full name for AQP2 and ENaC. Some typo such as Na,K-ATAse (Na,K-ATPase) should be corrected

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.