SUSTAINED HYPEROSMOLARITY LEADS TO THE EXPRESSION OF PROFIBROTIC FACTORS IN VIVO

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BACKGROUND

It has been shown in vitro, that acute changes in osmolarity induce the profibrotic early growth response factor-1 (Egr-1). However, its possible effect in the renal medulla is still unknown.
We therefore aimed to investigate the effects of sustained hyperosmolarity on the renal medullary Egr-1 expression.

METHODS

Animal model:
Adult male Sprague Dawley rats (n=6/group) were water restricted to 15ml/200g body weight per day (hyperosmolar) or treated with 15 mg/day furosemide (hyposmolar), both for 5 days. Controls had free access to water and rodent chow.

Experimantal groups:
1) Control (n=6)
2) Water restriction (n=6)
3) Furosemide (n=6)

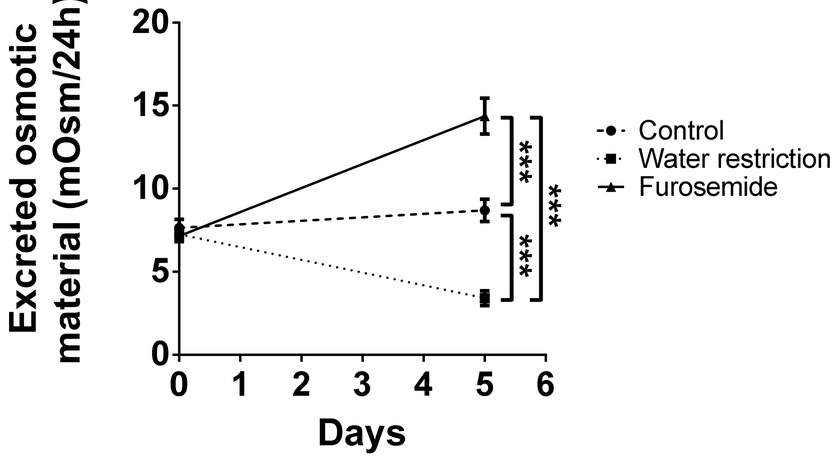
Performed analyses:
- Daily excreted osmotic material in the urine
- Renal medullary mRNA expression of
  - TGF-ß
  - Egr-1
  - cFos/cJun
  - TIMP-1
- Renal Egr-1 immunostaining

Statistics:
Data are presented as mean+/- SD. Kruskal-Wallis test was performed to test statistical significance.

RESULTS

Daily excreted osmotic material

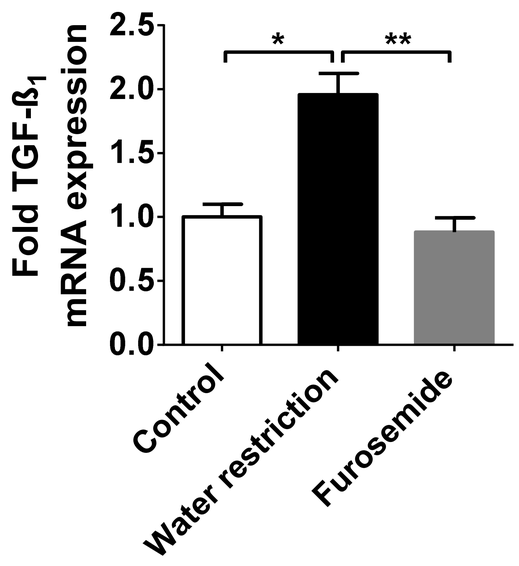
The amount of daily excreted osmotic material increased by 2-fold due to water restriction ($p<0.001$), but significantly decreased due to furosemide treatment.

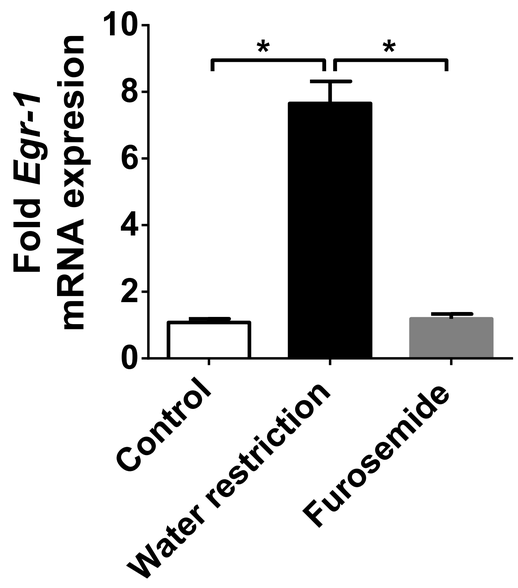


*** p<0.001

Medullary mRNA expressions

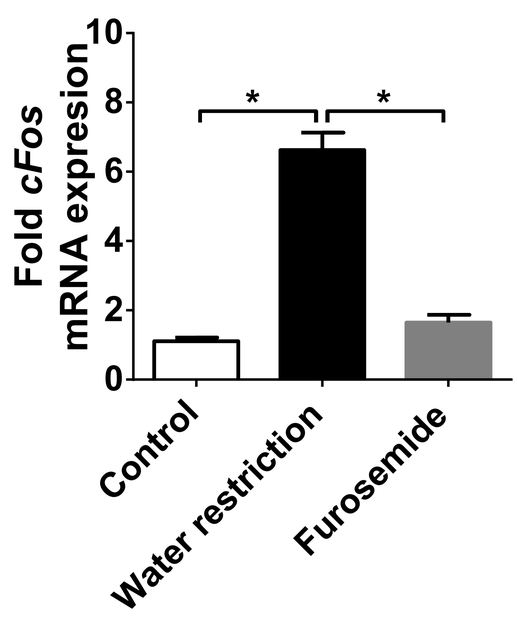
The mRNA expression of both profibrotic the TGF-ß and Egr-1 increased in the hyperosmolar medulla.

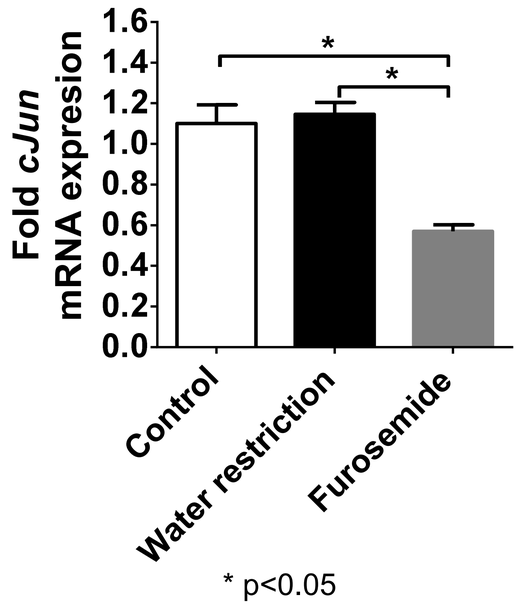




* p<0.05, *** p<0.01

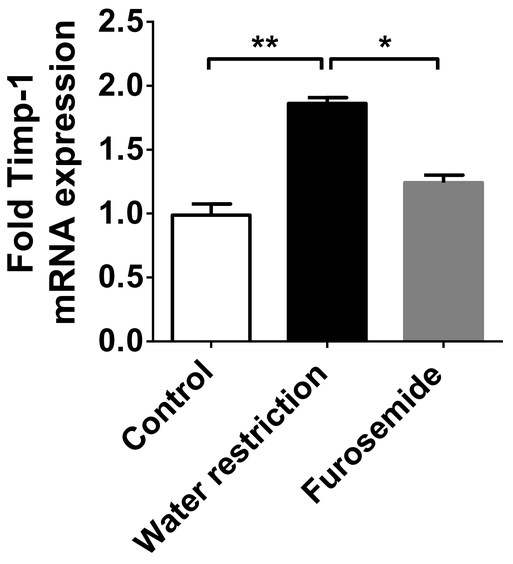
Although the expression of c-Fos increased by 6-fold in the water restricted medulla, it was not accompanied by c-Jun.





* p<0.05

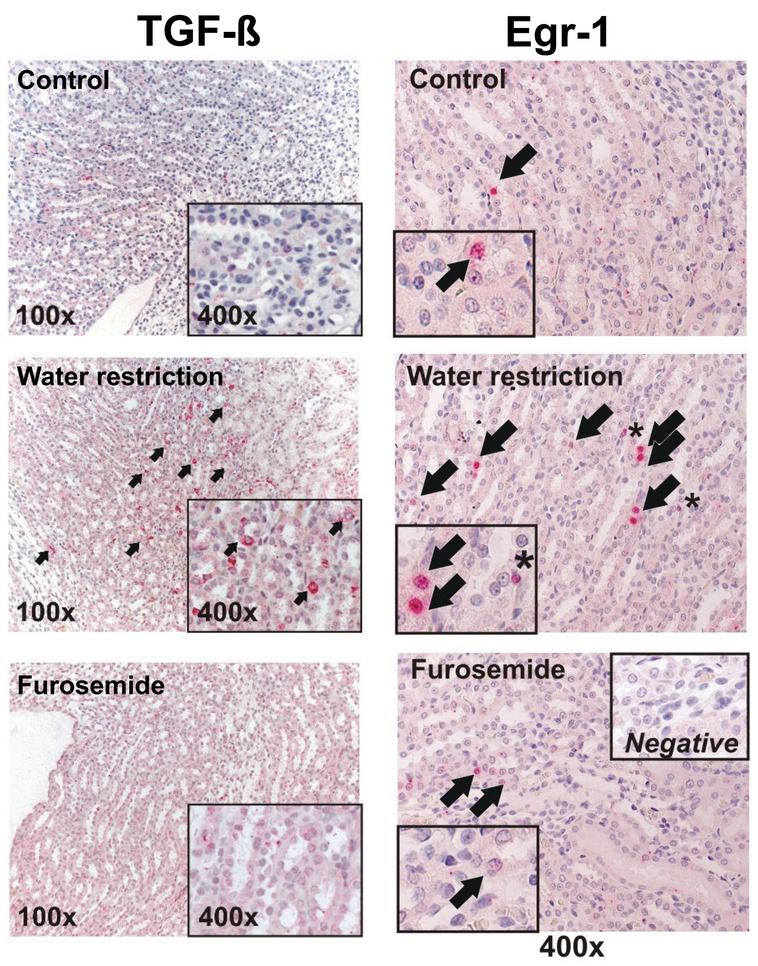
Water restriction also lead to increased mRNA expression of TIMP-1.



* p<0.05, *** p<0.01

TGF-ß and Egr-1 immunostaining

The outer medulla of water restricted rats stained positive for TGF-ß and Egr-1, whereas controls and furosemide treated rats depicted minimal staining.



CONCLUSION

We conclude that sustained hyperosmolarity might accelerate the development of interstitial fibrosis in the presence of kidney disease by the upregulation of TGF-ß and Egr-1 in the rat renal medulla, accompanied by increased TIMP-1.

FUNDING

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