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Blockade of CNG channels abrogates urethral relaxation induced by soluble guanylate cyclase activation

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In the present study, we have characterized the presence and distribution of cGMP-gated cationic channels (CNG) in the rat urethra as well as its putative role in the mediation of the nitrergic relaxation. Previous studies have shown the inhibition of the sheep urethral nitrergic relaxations by the CNG's inhibitor L-cis-diltiazem [1]. Also in the rat urethra, L-cis-diltiazem (50 μM) inhibited nitrergic relaxations elicited by electrical field stimulation (EFS) of arginine-vasopresin (AVP)-precontracted urethral preparations (Figure 1A).

This effect was stereoselective since the isomer D-cis-diltiazem did not have any effect on urethral relaxations. Similarly, L-cis-diltiazem (50 μM) showed a complete blockade of the relaxation induced by the addition of YC-1 (50 μM), an specific activator of the soluble guanylate cyclase (sGC) (Figure 1B), thus reinforcing that L-cis-diltiazem would be acting as specific inhibitor of CNG channels in this tissue.

The presence of these channels in urethral tissue was tested by carrying out conventional RT-PCR studies using retina as a positive control. A band of the predicted size showing after sequencing, a 99% identity with the rod-type CNGA1, together to a second band with a similar size to that ofthe CNGB1 fragment, were obtained. These results suggest that they are heteromeric retina-like CNG channels.

Immunofluorescence studies were performed to analyze the distribution of CNG immunoreactivity (-ir) in sections of the urethral wall. As can be seen in Figure 2, a strong CNG-ir was present in a subpopulation of vimentin-ir cells known as Interstitial Cells of Cajal (ICC), while

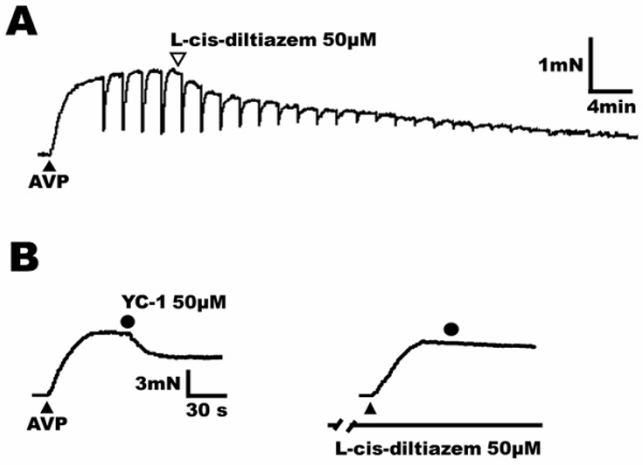

Figure 1
The presence of L-cis-diltiazem (50 μM) rapidly and effectively inhibited relaxation in arginine-vasopresin (AVP)-precontracted urethral preparations induced by both A) EFS (0.8 ms, 10 Hz, 5 s at 2 min-intervals) and B) guanylate cyclase activation by YC-1 (50 μM).

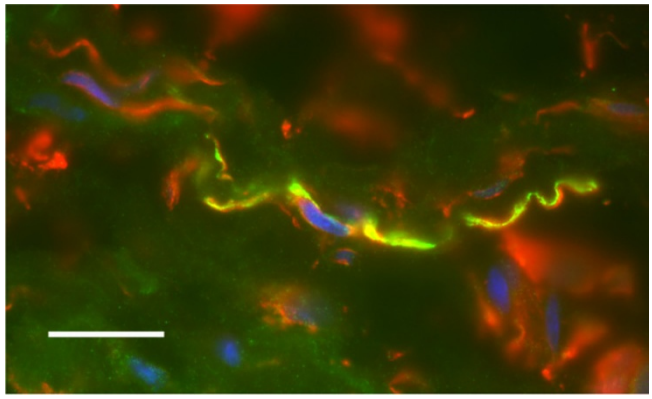

Figure 2
Section of rat urethra showing immunofluorescence for CNG1 channels (green) and vimentin (red) and its co-localization in a intramuscular Interstitial cell [nuclei are stained with DAPI (blue)]. Scale bar: 20 μm.

a fainter labeling was observed in smooth muscle cells (identified by actin-ir). CNG-ir was never observed in neural structures, nerve terminals, nerve trunks or ganglia. This pattern of CNG labeling and co-localization is similar to that described for the cGMP-ir found in the urethra upon functional nitrergic stimulation [2]. We suggest that CNG channels could be an essential ionic mechanism that would link activation of the NOS-GC pathway to relaxation. In addition, these results point to ICC as key elements in the mediation of the nitrergic urethral relaxation, although its precise role remains to be elucidated.

Acknowledgements

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References

1. Triguero D, González M, García-Pascual A, Costa G: **Atypical relaxation by scorpion venom in the lamb urethral smooth muscle involves both NO-dependent and -independent responses.** *Naunyn-Schmiedeberg's Arch Pharmacol* 2003, **361:**151-159.
2. García-Pascual A, Sancho M, Costa G, Triguero D: **Interstitial cells of Cajal in the urethra are cGMP-mediated targets of nitrergic neurotransmission.** *Am J Physiol Renal Physiol* 2008, **295:**F971-F983.

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