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EVIDENCE FOR PROSTAGLANDIN INVOLVEMENT IN NEURO-MODULATION IN THE GUINEA PIG BLADDER

Hypothesis / aims of study

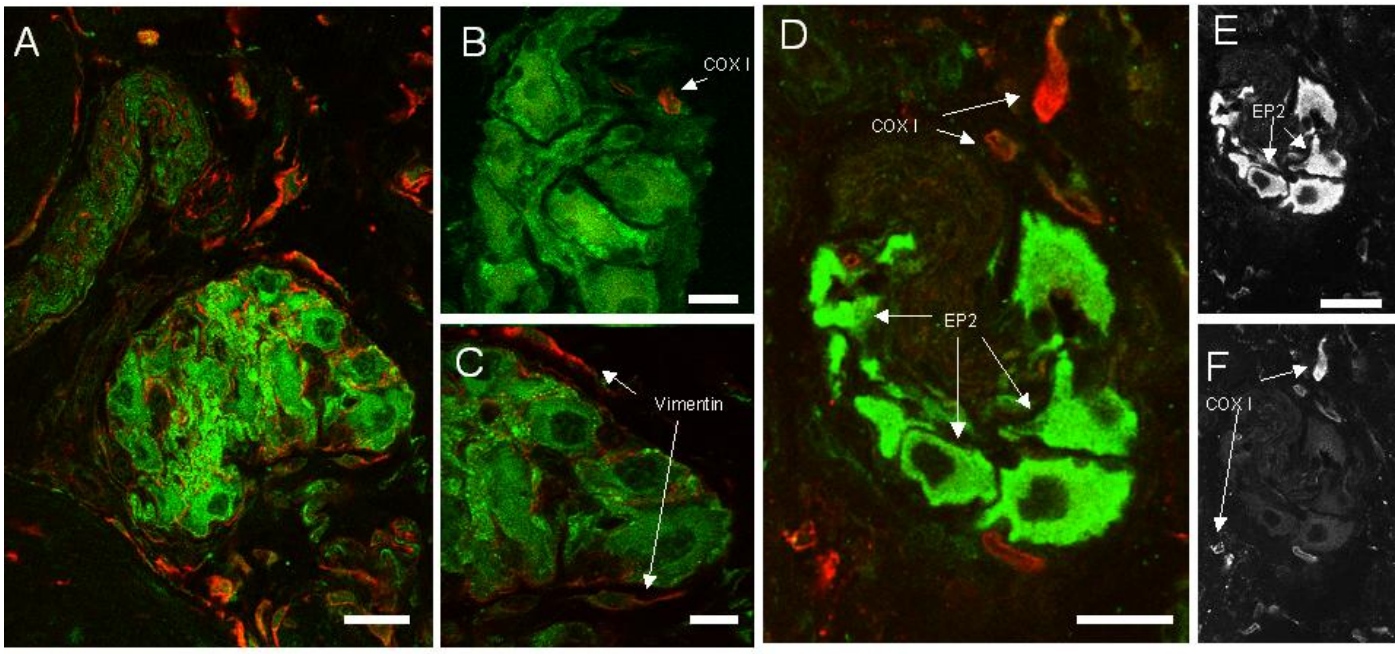
The mucosa and muscle layers of the bladder are reported to be capable of synthesizing and releasing prostaglandins (PG) in response to distension [1]. The functional role of this endogenous PG is not known but it has been suggested that it plays a role in urothelial signalling and muscle contraction. Ganglia are known to be present in the bladder wall of several species including human, pig and guinea-pig. In the human, the ganglia receive multiple synaptic contacts [2]. Their role has been assumed to be the relay of activity in the parasympathetic nerves to the smooth muscle to initiate micturition contraction. However, intramural ganglionic network has also been suggested to influence and regulate the motor/sensory system within the bladder wall [3]. In the present study we have explored the possibility that the ganglia may also be involved in the responsiveness of the bladder to PG.

Study design, materials and methods

Bladders from five male guinea pigs were killed by cervical dislocation and the bladders removed. Tissues were then fixed in 4% paraformaldehyde and processed for immunohistochemistry. Primary antibodies used were antibody to the prostaglandin type 1 receptor (EP1), vimentin and COX I. Specific antibody binding was visualised using the appropriate secondary antibodies. A blocking peptide was used to confirm the specificity of the EP1 antibody.

Results

Figure D-E illustrate our basic observation that intra-mural ganglia associated with the inner and outer muscle layers of the guinea pig bladder express receptors for prostaglandin receptors type 1 (EP1). Also, prostaglandin receptor type 2 (EP2) was detected on ganglionic neurones (Figure D-F). The source of the prostaglandin involved in activating these ganglionic receptors was explored using antibodies to the cyclo-oxygenase enzyme (COX I). COX I immuno-reactivity was observed in accessory cells close to the ganglia (Figure D-F). Based on vimentin staining these structures are likely to be interstitial cells. Blood vessels were regularly seen within the ganglia but no nerve fibres were seen that could be linked to prostaglandin production.



Localization of EP1 and EP2 in the intramural ganglia of the guinea pig bladder. EP1 staining in intramural ganglia of the guinea pig bladder.
Panel A shows an intramural ganglion stained with EP1 (Green) and Vimentin (red).
In panel B a ganglion in a different guinea pig bladder stained for EP1 (Green) and COX I (red) is shown.
Panel C shows a magnification of an EP1 positive (green) ganglion cell in a third bladder surrounded by Vimentin fibres (red).
Panel D shows an intramural ganglion with EP2 (green) and COX I (red).
Panels E and F show the individual stainings for EP2 and COX I respectively. Calibration bar: 10 µm.

Interpretation of results

These observations suggest that the ganglia in the bladder wall can respond to prostaglandins. The role of this input to the ganglia is not known. Similarly the source of the prostaglandin which might activate these receptors in vivo is not clear. Some prostaglandin may come from accessory cells, the intestinal cells. Alternatively, the prostaglandin may be delivered to the ganglia via their blood supply. It has been suggested that the neural networks involving the ganglia are involved in modulating motor activity associated with the motor component of motor/sensory noise. Activation of prostaglandin receptors on these neurons may therefore have an influence indirectly on bladder sensation. Such a mechanism may be important in the generation of bladder pain and increased sensations associated with bladder inflammation.

Concluding message

Functionally, the presence of EP1 and EP2 receptor in a ganglion and the possibility of prostaglandin production by COX I in their vicinity, suggests that intramural ganglia are involved in (pre)processing afferent information, part of which might be the control of spontaneous contractile activity in the smooth muscle as a motor-sensory system. Disruption of this motor-sensory system may be important in functional bladder problems, such as the overactive bladder syndrome.

References

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Specify source of funding or grant	**This Research was funded by an unconditional grant (Mozaiek) to Dr M.S. Rahnama'i by the Netherlands Organisation for Scietific Research (NWO)**
Is this a clinical trial?	**No**
What were the subjects in the study?	**ANIMAL**
Were guidelines for care and use of laboratory animals followed or ethical committee approval obtained?	**Yes**
Name of ethics committee	**Maastricht University Anmial Ethical Committee (DEC Universiteit Maastricht)**