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THE DISTRIBUTION OF SENSORY FIBRES IN THE MOUSE BLADDER: POSSIBLY DIFFERENT CLASSES OF SENSORY NERVES

Hypothesis / aims of study

Previous work on the guinea pig has demonstrated different types of sensory fibres in the urothelium [1]. The functional significance of these different fibres is not known. In future studies the mouse will be used to investigate the afferent activity of bladder nerves. Before such studies can be developed it is essential to know if there are different types of sensory nerves. The aim of this study was to describe the distribution of sensory fibres in the mouse bladder and to explore different populations sub-serving different sensory roles.

Study design, materials and methods

A total of 8 male mice were used in the study. The animals were killed by cervical dislocation, the bladders removed and washed in Kreb's solution at 36^{o}C, gassed with 95% O_2 and 5% CO_2. Tissues were then fixed in 4% paraformaldehyde and processed for immunohistochemistry. The identification of sensory fibres was based on the following criteria. (i) Nerves expressing caletonin gene related peptide (CGRP) were classified as sensory fibres. (ii) nerves in the lamina propria and associated with the urothelium were also classified as sensory. Primary antibodies used were to CGRP, to the non specific nerve marker PGP 9.5 and to the vesicular acetylcholine transporter (VAChT). Specific antibody binding was visualised using the appropriate secondary antibodies.

Results

CGRP-IR positive (CGRP^{+} immunoreactive) nerve fibres were found within the lamina propria and associated with the urothelium. In the bladder base these fibres were observed to penetrate the urothelium and lie between the basal epithelial cells. VAChT positive (VAChT^{+}) fibres were also found in the lamina propria but at lower density than the CGRP fibres. These VAChT^{+} fibres were only very rarely seen to penetrate the urothelium. A dense population of CGRP positive fibres was seen within the muscle bundles. These fibres were found at higher density within the inner muscle layers compared to the outer muscle layers.

Interpretation of results

These observations suggest that there are, at least, four distinct populations of sensory nerve in the wall of the mouse bladder: CGRP^{+} fibres within the urothelium (Figure 1), CGRP^{+} fibres within the lamina propria (Figure 1), VAChT^{+} fibres in the lamina propria (Figure 2) and CGRP^{+} fibres in the muscle layers (Figure 1). The observation of a higher density of presumptive sensory fibres in the inner muscle compared to the outer layer suggests that the inner muscle layer has different functional and sensory characteristics compared to the outer. The role of these different types of fibres is not known but they must contribute to different aspects of the afferent noise emanating from the bladder. For example the urothelial nerves may be sensitive to urothelial deformation and the substances released by the urothelium upon stretch. The different roles of CGRP^{+} and VAChT^{+} fibres is unknown. The physiological stimulus for the fibres in the muscle is not known but might be mechano-transduction in response to muscle stretch. The distribution and density of sensory innervation in the mouse is different from the guinea pig.

Concluding message

There are at least 4 different populations of sensory nerves in the wall of the mouse bladder. Furthermore the inner muscle is more densely innervated by sensory fibres. The appreciation and integration of this structural information and nerve classification is crucial for future studies on afferent electrical activity. In order to understand the physiological role of the activity in any particular nerve it is essential to know where that fibre originates and what types of fibres they are. The challenge is now to unravel the specific physiological roles of the different types of sensory fibres.

References

1. Cell and Tissue Research (2006) 325; 33-45.

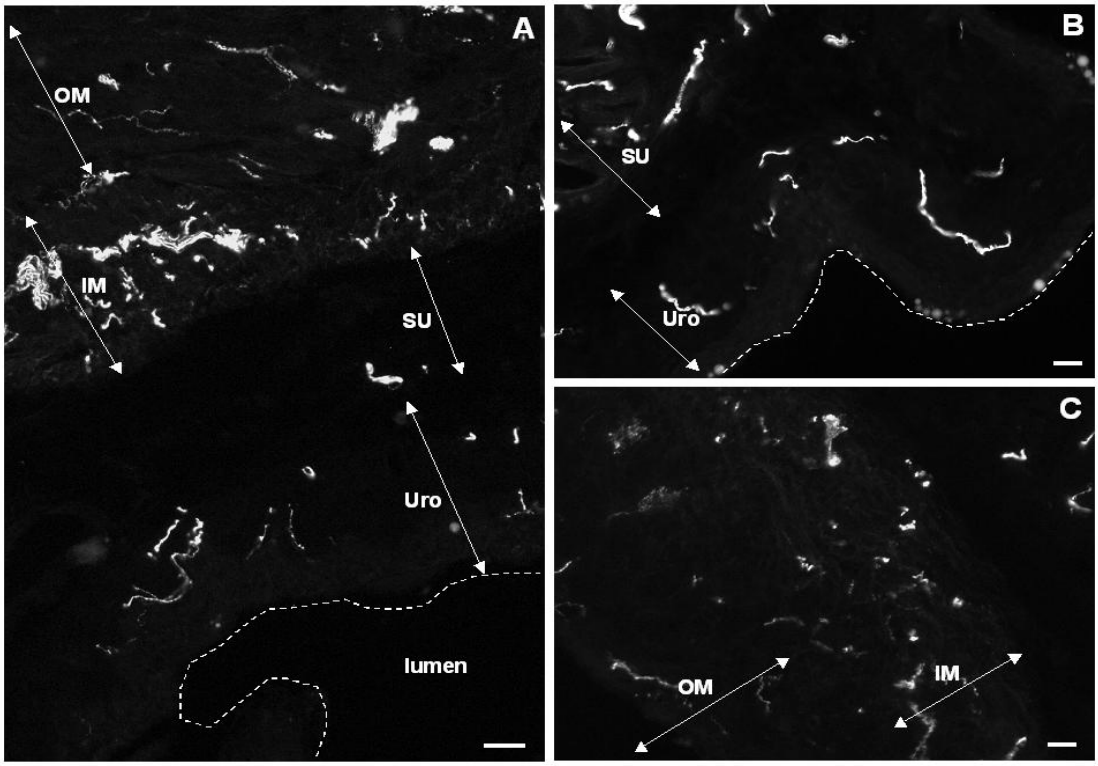

Figure 1: Location of CGRP positive fibers; Panel A shows CGRP-IR in the urothelium (Uro), suburothelium (SU) and muscle layers, note the dense innervation of the inner muscle (IM). Panel B shows CGRP fibres infiltrating the SU and urothelium. Panel C; points out the difference in inner and outer muscle (OM).

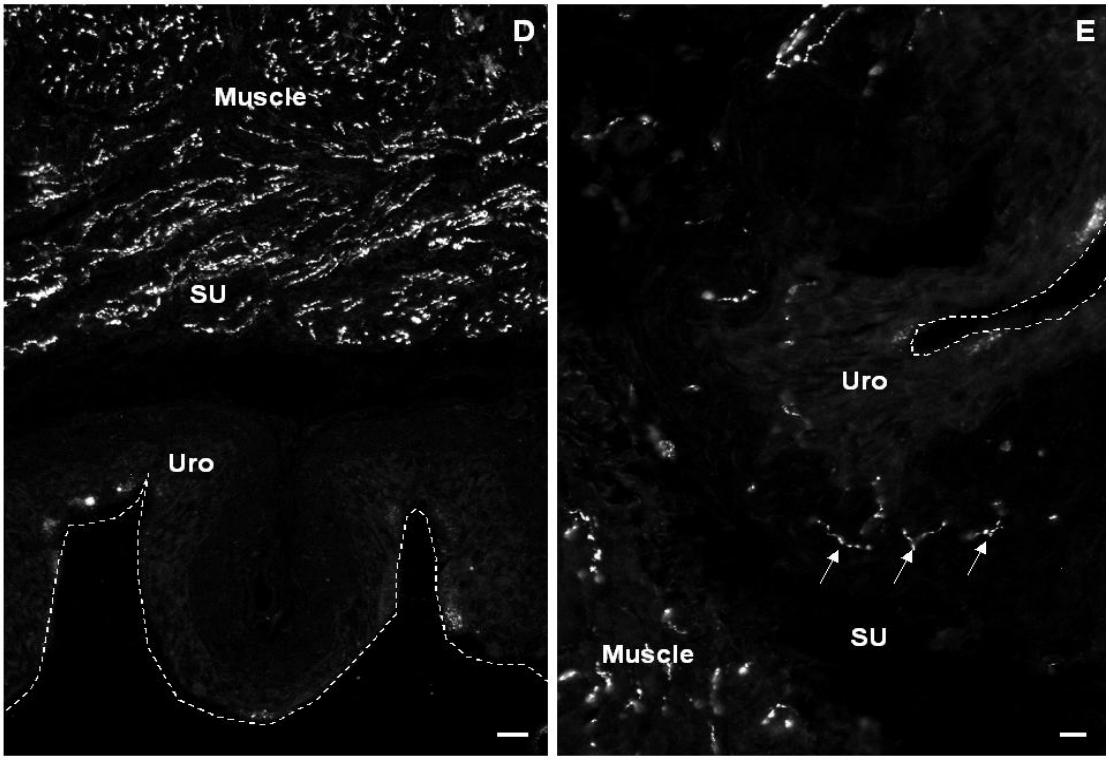

Figure 2: Location of VAChT positive fibres; Panel D shows abundant VAChT innervation of the inner and outer muscle, but almost no infiltration of the SU and Urothelium. Panel E shows some discrete VAChT fibre infiltration (arrows) in the urothelium and SU.

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