

## C-FIBERS MODULATE RELEASE OF MEDIATORS FROM THE EPITHELIUM, AND SPONTANEOUS CONTRACTIONS IN THE RAT BLADDER

### Hypothesis / aims of study

The acute release of neuropeptides (substance P, calcitonin gene-related peptide (CGRP), prostaglandin (PG) etc.) contained in peripheral sensory endings was shown to contribute to bladder activity and pain. Detrusor overactivity induced by PGE<sub>2</sub> and bradykinin (BK) has been reported to arise through bladder afferents [1, 2]. However, little is known about influences from bladder afferents to the bladder activity. In this study, we investigated the role of c-fibers in release of mediators from the epithelium or spontaneous contraction in the bladder.

### Study design, materials and methods

Whole urinary bladders with the urethra from resiniferatoxin (RTX)-treated or normal rats were removed. A catheter was inserted through the urethra and fixed. The bladder was fixed vertically in an organ bath with Krebs solution. Administrations of 0.3 mL Krebs solution (baseline), followed by 1.5 mL vehicle were carried out and maintained for 10 minutes, respectively. After Krebs solutions were collected by dropping in free-fall, the intravesical adenosine triphosphate (ATP), PGE<sub>2</sub> and nerve growth factor (NGF) amounts were measured. Also, the strips with or without bladder epithelium were made from the other RTX-treated or normal rats. The strips were set in tissue baths, and spontaneous contractions were recorded.

### Results

The ATP, PGE<sub>2</sub> and NGF releases from the bladder epithelium elicited by distension in RTX-treated rats decreased to 28, 56 and 37% of those in normal rats, respectively ( $p < 0.05$  for ATP and NGF). The frequency of spontaneous contractions in the strips in RTX-treated rats decreased to 73% of that in normal rats, irrespective of the presence or absence of bladder epithelium ( $p < 0.01$  for each). As well, the amplitude of spontaneous contractions in the strips in RTX-treated rats decreased to 68 or 26% of that in normal rats ( $p < 0.05$  or  $p < 0.01$  for the presence or absence of bladder epithelium). In addition, the levels of TrkA (NGF receptor mRNA), BKB1 (BK receptor) and CRLR (CGRP receptor) were reduced in the bladder urothelium of RTX-treated rats.

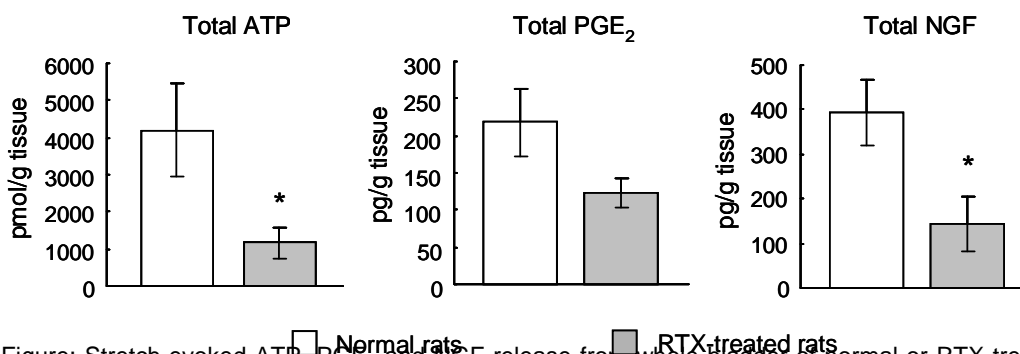


Figure: Stretch-evoked ATP, PGE<sub>2</sub> and NGF release from whole bladder of normal or RTX-treated rats. Values are shown as mean ± SE in 6 different bladders. \*  $p < 0.05$  : significant difference to normal rats (Student t-test).

### Interpretation of results

These results suggest that c-fiber afferents in the bladder influence the release of mediators from the epithelium and spontaneous contraction of the smooth muscle as well as transmission of perception into the central nerve system.

### Concluding message

C-fibers may modulate release of mediators from the epithelium, and spontaneous contractions in the rat bladder

### References

1. J Urol 177: 771, 2007
2. Neurosci Lett 262: 73, 1999

Specify source of funding or grant	None
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	University of Fukui Animal Care and Use Committee Guidelines