

STRETCH-INDUCED INCREASES IN THE SPONTANEOUS PHASIC CONTRACTILE ACTIVITY OF ISOLATED UROTHELIAL STRIPS INVOLVE MUSCARINIC RECEPTOR STIMULATION

Hypothesis / aims of study

Isolated strips of urothelium/suburothelium contract in response to neurokinin A (NKA) and these contractions are probably mediated via myofibroblasts [1]. The urothelium also generates its own spontaneous contractile activity which may be relevant to the development of bladder overactivity, where spontaneous bladder contractions occur during the filling phase. The aim of this study was to examine the effects of stretch on the spontaneous contractile frequency of the urothelium/suburothelium.

Study design, materials and methods

Isolated strips of pig bladder urothelium (including suburothelium) were set up in Krebs-bicarbonate solution at 37°C gassed with 5% CO₂ in oxygen and isometric tension recorded. The spontaneous rate of phasic contractions and the contraction amplitudes were recorded with tissues under 2g tension and then the effects of stretching the tissues was examined by increasing the tension on the tissues to 5g and then 10g tension. To assess the involvement of acetylcholine and muscarinic receptors in any responses, experiments were also performed in the presence of atropine (1µM).

Results

With tissues under 2g tension (n=8), urothelial strips spontaneously developed phasic contractile activity with a frequency of 4.1±0.2 contractions/minute and an amplitude of 0.48±0.14g. Stretching the urothelial strips until the tension increased to 5g resulted in an increase in spontaneous phasic contractile activity, the frequency increasing (P<0.05) to 5.5±0.2 contractions/min and contraction amplitude to 0.97±0.22g. Further stretching until the tension on the tissues was 10g, resulted in a further increase (P<0.05) in frequency to 6.1±0.2 contractions/min and increased the amplitude of contractions to 2.99±0.20g.

Identical experiments (n=8) were performed in the presence of the muscarinic receptor antagonist atropine (3µM). In the presence of this muscarinic receptor antagonist stretching the tissues did not alter the spontaneous rate of contractions (3.5±0.6, 3.6±0.5 and 3.7±0.6 contractions/min at 2g, 5g and 10g respectively). Similarly, in the presence of atropine, stretch had no effect on the amplitude of contractions.

Interpretation of results

This study demonstrates that the urothelium/suburothelium is able to spontaneously generate its own phasic contractile activity. Progressive stretching of these tissues increases the spontaneous frequency of contraction, but this stretch-induced effect could be antagonized with the muscarinic receptor antagonist atropine which completely abolished the stretch-induced increase in spontaneous contractile frequency.

Concluding message

It has been reported that stretch of the urothelium causes the release of acetylcholine [2] and these results suggest that this mechanism may operate to increase urothelial spontaneous contractile activity. This finding may be relevant to the spontaneous contractile activity observed in the overactive bladder, the urothelium possibly driving muscle contractions in the diseased state.

References

1. Sadananda, P., Chess-Williams, R. and Burcher, E. (2008) Contractile properties of the pig bladder mucosa in response to neurokinin A: a role for myofibroblasts. *Br. J. Pharmacol.* 153(7):1465-73.
2. Yoshida M, Inadome A, Maeda Y, Satoji Y, Masunaga K, Sugiyama Y, Murakami S. (2006) Non-neuronal cholinergic system in human bladder urothelium. *Urology* 67(2), 425-30.

Specify source of funding or grant	Supported by the NHMRC and a Pfizer OAB competitive Grant
Is this a clinical trial?	No
What were the subjects in the study?	NONE