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THE INFLUENCE OF NEUROKININ A ON PURINERGIC AND MUSCARINIC RECEPTOR SIGNALLING IN THE BLADDER

Hypothesis / aims of study

Neurokinin A (NKA) potentiates the contraction of bladder detrusor smooth muscle to ATP without affecting responses to muscarinic receptor stimulation [1]. Recently, the urothelium (urothelium plus suburothelium) has also been shown to contract in response to ATP [2] and NKA [3]. The aim of the present study was to determine whether the potentiating effect of NKA on ATP responses is also observed in the urothelium. The effect of NKA on cholinergic responses was also investigated.

Study design, materials and methods

Bladders were obtained from pigs at the local abattoir. Tissue samples were taken from the bladder dome and carefully dissected to separate the urothelium from the underlying detrusor. Strips of urothelium and detrusor were mounted under 2g tension in organ baths containing Krebs bicarbonate solution, gassed with 5% CO_2 in oxygen at 37^{O}C. Isometric developed tension was recorded as tissues were exposed to adenosine triphosphate (ATP) (1mM), followed by a single dose of carbachol (1µM) after wash-out when tension had returned to baseline. Tissues were then incubated with NKA (100nM) until tension was stable, before repeating single doses of ATP (1mM) and carbachol (1µm). Control experiments were also performed without the addition of NKA. Responses are expressed as the change in developed tension (g). Statistical differences between first and second responses to ATP and carbachol were analysed using the Student's paired t-test.

Results

ATP (1mM) induced contractions of a similar magnitude in strips of urothelium and detrusor smooth muscle (0.88 ± 0.08 (n=24) and 1.09 ± 0.20 (n=15) respectively). Contractions to carbachol (1µm) were also not significantly different between strips of urothelium and detrusor muscle (4.58 ± 0.27 (n=24) and 5.91 ± 1.41 (n=14) respectively).

The presence of NKA (100nM) significantly ***potentiated*** the responses to ATP in strips of urothelium and detrusor (Table 1), however this enhancement was greater (P<0.01) in detrusor compared to urothelium (226 ± 56% and 52 ± 17% increase in response respectively).

In contrast, the presence of NKA (100nM) was not associated with an enhancement of responses to carbachol and in the urothelium, a significant ***depression*** of contractile responses to carbachol was observed (Table 1).

		Mean change in tension ± SEM (g)	
	Before/After NKA (100nM)	Urothelium	Detrusor
ATP (1mM)	Before NKA	1.01 ± 0.12 (n=12)	1.45 ± 0.38 (n=8)
	After NKA	1.51 ± 0.23* (n=12)	4.32 ± 0.92** (n=8)
Carbachol (1µm)	Before NKA	4.36 ± 0.31 (n=12)	5.67 ± 1.55 (n=8)
	After NKA	2.39 ± 0.40** (n=12)	7.46 ± 1.32 (n=8)

Table 1. The influence of NKA (100nM) on the contractile responses of the bladder urothelium and detrusor *P<0.05, *P<0.001 compared with same tissue before exposure to NKA.

Interpretation of results

These data suggest that synergistic interactions between the tachykinin and purinergic systems may be important in regulating contractile responses of the bladder urothelium and detrusor. Surprisingly, the effect of NKA on cholinergic responses was depressant and this effect was limited to the urothelium.

Concluding message

The sensory neuropeptide NKA modulates cholinergic and purinergic responses of the bladder. The effects of the peptide are different on the detrusor smooth muscle and urothelium, but the relevance of these interactions to bladder function requires further investigation.

References

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