

## INHIBITION OF NON MICTURITION ACTIVITY BY CALCETONIN GENE RELATED PEPTIDE

### Hypothesis / aims of study

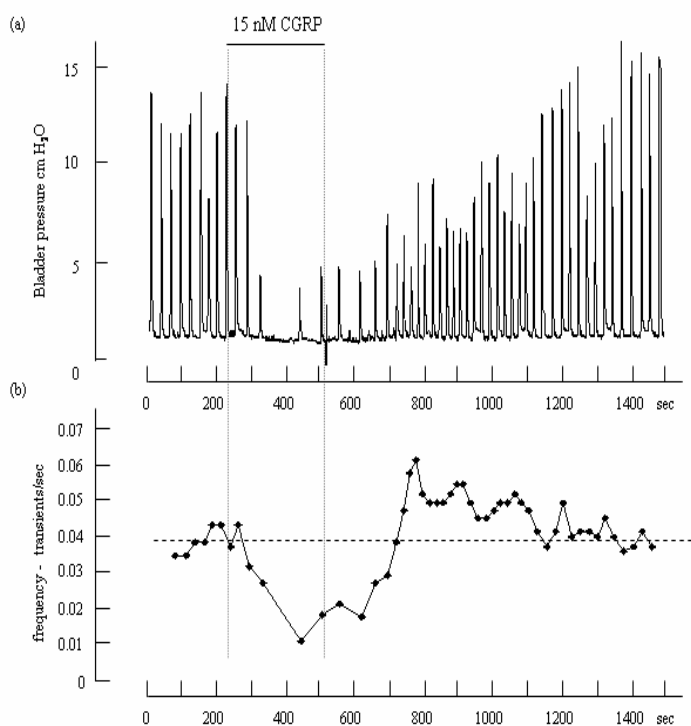
The physiological role of calcitonin gene related peptide in the bladder is unknown. The aim of the present work was to explore the actions of calcitonin gene related peptide (CGRP) on the isolated bladder and examine the hypothesis that CGRP inhibits non micturition activity.

### Study design, materials and methods

All of the experiments were done on the isolated whole bladders of guinea pigs. Complex integrated physiological responses can be initiated within the isolated bladder wall which may play an role in the generation of bladder sensations (1). Such responses, involving propagating waves of contraction and local stretches, can be influenced nerve stimulation and by direct application of neurotransmitter substances (2,3). The suburothelial layer in the bladder wall is profusely innervated by nerves containing CGRP the function of which are unknown. The experiments examine the effects of CGRP on non micturition activity.

### Results

Phasic activity was generated in bladders using the muscarinic agonist arecaidine (100 nM). CGRP was added to the abluminal solution bathing the bladders and changes in the activity noted. Figure 1 shows a typical response. On application of CGRP there was a rapid fall in the frequency and amplitude of the phasic activity which was slowly reversed on its removal. During the recovery phase a transient rise in frequency was noted. Exposure to lower doses of CGRP (1 and 3 nM) caused similar but weaker effects while higher concentrations (20 and 30 nM) completely inhibited phasic activity.



**Figure 1.** A shows typical responses of a guinea pig whole bladder preparation stimulated with 100 nM arecaidine to produce phasic activity. Where indicated by the horizontal bar 15 nM CGRP was added. B shows an analysis of the data illustrating the changes in frequency of the transients. These responses were seen in 7 other preparations.

### **Interpretation of results**

These data demonstrate a profound inhibitory action of CGRP on non micturition activity and suggest an inhibitory role for the CGRP innervation of the bladder wall. It has been suggested that nerve mediated regulation of phasic activity is an integral part of a complex physiological system within the bladder wall involved in the generation and modulation of afferent discharges and the generation of bladder sensations. The present data suggest the presence of a peptidergic neural inhibitory input to this system. CGRP containing neurones are found predominantly in the sub urothelial layer. This may suggest that the cellular components located in the sub urothelial space, the urothelium and sub urothelial cellular network, may play a role in the integration of input generating non micturition activity.

### **Concluding message**

It can be speculated that a neural inhibition of non micturition activity may represent a means to reduce bladder sensations by an entirely peripheral mechanism.

### **References**

1. Gillespie JI. The Autonomous Bladder: A View of the Origin of Bladder Overactivity. *BJU Int* 2004 *in press*.
2. Gillespie JI. Modulation of Autonomous Contractile Activity in the Isolated Whole Bladder of the Guinea Pig. *BJU Int* 2004, 93: 393-400.
3. Gillespie JI. Noradrenaline Inhibits Autonomous Activity in the Isolated Guinea Pig Bladder. *BJU Int* 2004: 93: 401-409.