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LUMBOSACRAL NEURONAL ACTIVITY IS ENHANCED FROM ACTIVATION OF UROTHELIAL PURINERGIC RECEPTORS

Hypothesis / aims of study- Urothelial purinergic receptors are important for the regulation of afferent sensory pathways in bladder pain and overactivity. Using in vivo electrophysiological recordings we evaluated the activity of spinal dorsal horn neurons in female rats at the L6/S1 level when urinary bladder pressure was abruptly increased. Intravesical infusion of ATP and systemic application of suramin allowed us to evaluate the contribution of urothelial purinergic receptors.

Study design, materials and methods- Rats were anesthetized with isofluorane. Suprapubic, venous and tracheal catheters were implanted. Laminectomy was performed at the L6-S1 spinal levels. The cervical spinal cord was transected, and rats were mechanically pithed. Anesthesia was stopped, rats were ventilated, and a muscle relaxant was administered. Bladder pressure was monitored and an AC amplifier was used for neural activity acquisition at 10 KHz via a tungsten electrode inserted into the dorsal horn. We evaluated field potentials during intravesical pressure steps ranging from 0-60 cm/H2O in A) control (saline in the bladder), B) after stimulation of urothelial purinergic receptors (1mM vesical ATP) and C) after the intravenous application of suramin (100 mg/kg). Pressure steps were maintained for one minute following by three minutes for recovery.

Results- Only neurons that showed an increased activity during bladder distention were evaluated. Under saline control conditions, the generation of field potentials increased concomitantly with bladder pressure steps, showing an activity change threshold between 20 and 40 cm/H2O. Intravesical application of 1mM ATP produced an increase in baseline activity, indicative of noxious stimulation, and activity increased above 40 cm/H2O pressure. Systemic suramin prevented the increase in neural activity in response to pressure changes, even after intravesical ATP. At a pressure of 60 cm/H2O, the frequency of the afferent responses was (potentials/20 s): 769.2+/-45 in saline, 1057.0+/-103 following intravesical ATP, and 203.8+/-78 following suramin injection.

Interpretation of results- These results suggest that urothelial purinergic receptors are important modulators of lumbosacral dorsal spinal neuronal activity. The inhibitory effects of suramin imply that enhanced lumbosacral neuronal signals result from activation of C-fibers during noxious bladder stimulation.

Concluding message-Purinergic receptors modulate sensory input from the bladder. Future purinergic antagonist could play an important role in treating detrusor overactivity.

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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	**Baylor Ethics Committee**