Conclusions

The present data suggest that the increased level of PGE_2 in the bladder contributes to the detrusor hyperreflexia in the chronic spinal rats, and that PGE_2 receptors antagonist reduced the hyperreflexia without decrease in the micturition pressure. This may lead to a new therapeutic potential using PGE_2 receptors antagonist for overactive bladder.

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None

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Title (type in CAPITAL LETTERS, leave one blank line before the text)
CYSTOMETRIC STUDIES IN CONSCIOUS P2X3 KNOCKOUT MICE REVEAL URINARY BLADDER HYPOREFLXIA

Aims of Study:

P2X3 is a ligand-gated channel expressed by small-diameter sensory neurons and is present in nerve bundles within detrusor muscle layers (1, 2). Endogenous ATP, released during bladder distension, may be responsible for 50-75% of the afferent nerve response to filling (3). In this study, urodynamic studies in conscious P2X3 knockout ($P2X3^{-/-}$) mice were conducted to investigate the role of P2X3 receptors in urine storage and voiding reflexes.

Methods:

Adult (5-6 months) male and female C57BL/6 (n=7), 129Sv (n=6), $P2X3^{-/-}$ (n=8) and $P2X3^{+/+}$ (n=8) as well as young (2 months) male $P2X3^{-/-}$ (n=6) and $P2X3^{+/+}$ (n=6) mice were studied. Cystometry was conducted 7 days after surgical placement and exteriorization of a urinary bladder catheter. Each mouse was placed in a metabolic cage, and saline was infused into the bladder (3ml/h). Urinary bladder pressures, void intervals, and void volumes were recorded using a Grass polygraph.

Results:

$P2X3^{-/-}$ mice had significantly increased urinary bladder capacity and decreased micturition frequency compared to $P2X3^{+/+}$ mice (Figure 1). There were no significant cystometric differences between male and female $P2X3^{-/-}$ mice. Mean void volumes (ml) were 0.41±0.04 and 0.23±0.02 and void intervals (min) were 9.0±0.8 and 5.3±0.3 in $P2X3^{-/-}$ and $P2X3^{+/+}$ mice, respectively ($p<0.01$, Figure 2). Similar results were obtained when $P2X3^{-/-}$mice were compared to C57BL/6 and 129Sv parental strains ($p<0.01$, Figure 2). Baseline, threshold, and micturition pressures were not significantly different between $P2X3^{-/-}$ and $P2X3^{+/+}$ mice. There were also no significant cystometric differences between young $P2X3^{-/-}$ and $P2X3^{+/+}$ mice.

Conclusions:

$P2X3^{-/-}$ mice (5-6 months old) have significantly increased urinary bladder filling capacity and decreased micturation frequency, suggesting that P2X3 receptors play an important role in urinary bladder sensory activity. The increased urinary bladder capacity was not apparent in young $P2X3^{-/-}$ mice (2 months old), suggesting that this bladder dysfunction develops over time. Given these findings, it is proposed that P2X3 antagonists may be useful in the treatment of conditions of poor bladder compliance, e.g., overactive bladder.

Figure 1

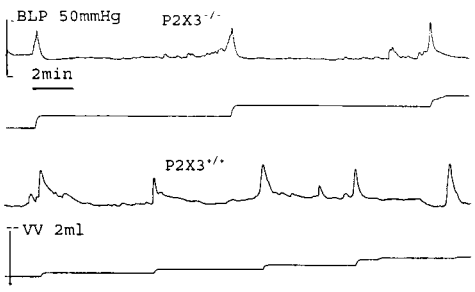
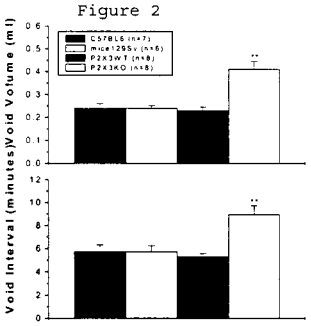


Figure 2



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Title (type in CAPITAL LETTERS, leave one blank line before the text):

A POSITRON EMISSION TOMOGRAPHY (PET) STUDY ON BRAIN CONTROL OF URINE STORAGE IN HUMANS

Aims of study It is broadly accepted that the brain control is crucial to maintain the urinary continence. In fact patients with cerebrovascular disease often have urge incontinence. However, little is known regarding which lesions in the brain cause such urine storage dysfunction in human. As the first step to answer this question, this study was performed to clarify the human brain regions involved in the voluntary urine storage, using positron emission tomography (PET).

Methods Brain activation was measured in male healthy and right-handed volunteers (n=8, age range 27-41, mean age 33 years). With the head fixed in an air-pressured mold, the subjects were placed in a horizontal position in the PET camera (ECAT EXACT HR+, Siemens-CTI, TN, USA). Beforehand 8 Fr. catheter was indwelled in each subject and the bladder was made empty. A