ALPHA-1 ANTAGONISTS INHIBIT THE PRIMARY AFFERENT ACTIVITY FROM THE IRRITATIVE BLADDER OF THE RAT.

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Hypothesis / aims of study
Many reports show alpha-1 effects in the efferent systems to the urinary bladder. Alpha-1 facilitation for micturition reflex has been reported in the preganglionic neurons of spinal cord, in the pelvic ganglia and in the detrusor smooth muscle. Recently, a theory is coming out that alpha-1 antagonists inhibit the afferent limb in the lumbosacral cord (1). Then, we interested whether or not alpha-1 antagonist effects in the afferent systems. Many clinical data indicate alpha-1 antagonists tend to improve the irritative symptoms as well as obstructive symptoms. These data also suggest alpha-1 antagonist might act on the primary afferent systems, not only on the spinal cord. Since alpha-1 receptors were not identified at the primary afferent neurons, alpha-1 agonist and/or antagonist might act on the uroepitherium and nearby structures. Anyway, we examined the effects of alpha-1 antagonist on single unit-recording from the bladder afferent fibers in vivo.

Study design, materials and methods
We used Wistar female rats for these experiments (n=28). Rats were anesthetized by 0.9-1.0 mg/kg (i.p.) urethane. Double lumen catheter was inserted into the urinary bladder from external urethral orifice for infusion and recording the vesical pressure. Then, L3-L6 vertebrae were exposed and we selected very fine filament of the L6 dorsal root for recording the afferent activity from the pelvic viscera. We used alpha-1 antagonists, naftopidil (0.75-1.66 mg/kg) and tamsulosin (0.0001-0.01 mg/kg) for these experiments. Drugs were administered intravenously into the external jugular vein. Unit-recording was digitalized with AD converter and recorded in Power Lab System (version 5.0). The numbers of spikes/sec were counted with window discriminator.

Results
Naftopidil (1 mg/kg, i.v.) inhibited the rhythmic bladder contraction in constant volume condition. The effect was appeared at 5-10 minutes and complete inhibition was observed for 20-50 minutes. When recovery appeared, frequency of contraction (22±4.2 /h) and maximum contraction pressure (32±2.4 cmH2O) was same as control. Naftopidil (1.0 mg/kg, i.v.) increased the latency of bladder contraction for 180±12 % in single cystometrogram (CMG, n=3). Intercontraction interval was prolonged to 210±15 % when we used continuous CMG (n=4).