11 Bladder primary afferent pathways to the spinal cord in mice

Eur Urol Suppl 2019; 18(1);e16

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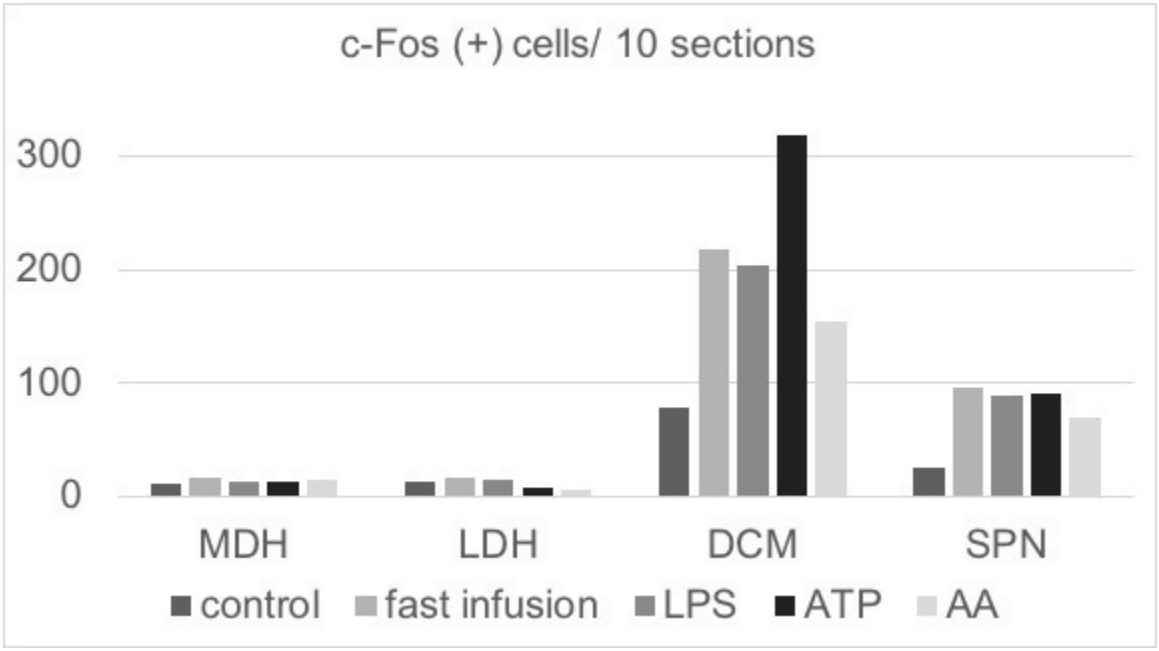
Introduction & Objectives: Mechanical or chemical stimuli to the bladder is transferred via bladder primary afferent nerves to the spinal cord. The spinal neurons projected from these primary afferent nerves are considered to be involved in processing input from the bladder. Medial dorsal horn (MDH), lateral dorsal horn (LDH), dorsal commissure (DCM), and sacral parasympathetic nucleus (SPN) of the spinal cord have been reported to have projections from the bladder afferent nerves in cats and rats. However, little has been known in mice. The aim of this study is to identify the bladder primary afferent pathways to the spinal cord in mice.

Materials & Methods: Male C57BL/6J mice were used. First, neuronal tracing study was performed by using bidirectional neuron tracer Cholera toxin B (CTB). One week after CTB injection into bladder wall, the spinal cord was dissected and the distribution of CTB in the L6-S1 spinal cord was analyzed. Next, spinal *c-fos* expression study was performed. In continuous cystometry under urethane anesthesia, saline 1.5ml/h (control), saline 12.0ml/h (fast infusion), 1g/ml lipopolysaccharide 1.5ml/h (LPS), 50mM adenosine triphosphate 1.5ml/h (ATP), and 0.5% acetic asid 1.5ml/h (AA) were continuously infused into the bladder for 2 hours. The c-Fos (+) cells in the L6-S1 spinal cord were counted in four spinal cord regions: MDH, LDH, DCM, and SPN.

Results: CTB positive nerve fibers were distributed to LDH, SPN, and DCM. These findings suggested that afferent pathways from the bladder project in these areas of the spinal cord in mice. The count of c-Fos (+) cells/ 10 sections was 11.3±2.3, 17.5±6.2, 12.6±1.9, 12.8±5.2, and 15.3±1.2 in MDH; 14±2.2, 17.5±3.5, 15.8±2.0, 8.6±1.2, and 6.7±0.7 in LDH; 78±22, 219±26, 203±21, 318±24, and 155±1.7 in DCM; 26±5.6, 96±24, 89±19, 90±7.5, and 69±11 in SPN (control, fast infusion, LPS, ATP, and AA group, respectively, means±SEM). Both mechanical stimuli by fast infusion and chemical stimuli by LPS, ATP, and AA were revealed to increase the c-Fos (+) cells in DCM and SPN of the L6-S1 spinal cord in mice. This

finding is not consistent with that of cat and rat, because noxious stimuli has been reported to increase the c-Fos (+) cells in MDH, SPN, and DCM.



Conclusions: Mouse bladder primary afferent pathways are suggested to project to the spinal neurons of DCM and SPN but not of MDH and LDH. Spinal neurons of DCM and SPN are considered to be involved in processing various input from the bladder in mice.