INTRODUCTION:
Compression of cauda equina by lumbar spinal canal stenosis is a major clinical problem associated with intermittent claudication. In an experimental spinal stenosis model, Schwann cells and glia in the cauda equina and spinal cord were activated to produce TNF, and induce neuropathic pain and motor dysfunction. To decrease the hypalgesia and motor dysfunction, TNF is a target for the therapy. However, TNF inhibitor administration may exacerbate heart failure, and there appears to be a higher incidence of serious infections.

Rho, a member of the small GTPases, is activated by TNF and induces TNF, suggesting that it has an important role in pain transmission and nerve degeneration in the cauda equina and spinal dorsal horn. However, the role of Rho kinase in cauda equina and spinal cord has not been clarified.

The purpose of this study was to investigate activation of Rho kinase in cauda equina compression, and effect of epidural administration of Rho kinase inhibitor, and on motor function after cauda equina compression by spinal canal stenosis.

METHODS:
Immunohistochemical and behavioral study using a rat model of cauda equina compression. Twenty-seven 6-week-old male Sprague-Dawley rats (200–250 g) were anesthetized with sodium pentobarbital (40 mg/kg, i.p.). For spinal canal stenosis, a piece of silicon (4 mm long, 1 mm wide; Sec. 1 mm thick) was placed under the lamina of the 3rd lumbar vertebra (SCS group; n = 18). We divided the SCS group into 2 subgroups: rats from one group were fitted with an osmotic minipump filled with Rho inhibitor, and rats from the other group were injected with the same volume of 0.9% Saline. In the sham-operated group, laminectomies were performed at L4 (laminectomy group; n = 9). We examined mechanical allodynia and motor function using von Frey hairs, treadmill and immunohistochemically localized Rho in the cauda equina and spinal cord, double staining with Neurofilament (marker for neurons and nerve fibers). We also examined the effects of epidural administered Rho kinase inhibitor on hypoalgesia and motor dysfunction after spinal canal stenosis.

All protocols for animal procedures in these experiments were approved by the ethics committees of our institutions following National Institute of Health Guidelines for the Care and Use of Laboratory Animals (1996 revision).

RESULTS:
In the SCS group significant mechanical hypoalgesia was observed compared with the laminectomy group. Walking duration in the SCS group was significantly less than that in the laminectomy group. Mechanical hypoalgesia in the SCS group recovered after continuous epidural administration of Rho inhibitor. Walking duration after injection of Rho inhibitor in the SCS group was significantly longer than that in the SCS group without injection of Rho inhibitor.

We demonstrated that activated Rho kinase activated cells in spinal cord and cauda equina were not observed before spinal canal stenosis. Rho kinase activated cells also emerged in the spinal cord and cauda equina after spinal canal stenosis. Epidural administration of Rho kinase inhibitor improved hypoalgesia and walking duration after spinal canal stenosis.

CONCLUSIONS:
These findings suggested that activated Rho may play an important role in nerve degeneration of cauda equina in spinal canal stenosis. We demonstrated that an inhibitor of Rho might be a useful agent in spinal canal stenosis.