INTRODUCTION:
Radicular pain is one of the most common complaints handled by orthopedic surgeon. As the cause of sciatica, the mechanical compression of the nerve root and the chemical reactions induced by herniated disc containing nucleus pulposus have been reported. However, the pathological mechanism is still unknown. On the other hand, neuropathic pain followed by peripheral nerve injury is considered that there are two types of pain state; sympathetically independent pain (SIP) and sympathetically maintained pain (SMP) that is attenuated by sympathectomy or sympathetic nerve block. Recent immunohistological studies in a peripheral nerve injury model have shown that sympathetic nerve fibers sprout the neurons in dorsal root ganglion (DRG). This abnormal sympathetic-somatosensory interaction seems to lead SMP. Also the sympathetic nervous system is suggested to be concerned in the radicular pain for the clinical effectiveness of the sympathetic block on radicular pain. The purpose of this study is to elucidate the pathological mechanism of radicular pain by investigating pain-related behavior of lumbar root constriction model in the rat. Furthermore, to assess the influences of sympathetic nerve fiber to radicular pain, we performed immunohistological analysis using antibodies to tyrosine hydroxylase.

MATERIALS & METHODS:
Male Sprague-Dawley rats (200-250g) were used. In lumbar root constriction group (n=22), the left L5 spinal root was exposed and ligated tightly with 8-0 nylon suture. While in sham group (n=12), the left L5 nerve root was exposed only without the ligation. Non-operated rats were used as a control group (n=6).

1. Behavioral testing
Behavioral testing was performed before and after the operation on 3, 7, 10, 14, 21, 28 days. Mechanical stimulation was applied 30 times on the hind paw with Semmes-Weinstein monofilaments (1.2g, 11.3g). Mechanical threshold was presented as withdrawal frequency of the rat hind paw. Noxious radiant heat as thermal stimulation was applied likely and withdrawal latency was measured. We compared three groups with the withdrawal frequency and latency, calculated the difference of ipsilateral and contralateral side.

2. Immunohistochemistry
At the end of behavioral testing period, the animals were deeply anesthetized with an intraperitoneal injection of sodium pentobarbital (60mg/kg). Bilateral DRGs and spinal roots (L4 and L5) were removed and then were frozen in mold and sectioned on a cryostat (8-10μm). The sympathetic fibers in the DRG were immunostained with antibodies to transmitter-synthesizing enzyme tyrosine hydroxylase (TH) according to the ABC method.

RESULTS:
1. Behavioral testing
Mechanical allodynia and thermal hyperalgesia were markedly observed in the root constriction group compared with sham or control group (p<0.001, Fig.1, 2). In ipsilateral hind paw, significant increases in withdrawal frequency and decreases in withdrawal latency were measured from 3 days after the operation and maintained up to 28 days. The increases in withdrawal frequency were flattened at 7 days after the operation, and the decreases in withdrawal latency were flattened at 3 days after the operation. No significant differences were seen between two kinds of Semmes-Weinstein monofilaments.

2. Immunohistochemistry
28 days after the operation, TH-immunoreactive fibers were scarce in the DRG on the contralateral side as in the DRG of a sham operated and control rat. On the other hand, TH-immunoreactive fibers were more abundant in ipsilateral L4 and L5 DRGs compared with contralateral DRGs. TH-immunoreactive fibers could not be found around the DRG neuron soma, but could be found around the myelin sheath in the DRG. Sympathetic axons grow along dorsal root following nerve root constriction. There was no difference of axon type between ipsi- and contralateral side (Fig.3).

DISCUSSION:
As well as peripheral nerve injury model, mechanical allodynia and thermal hyperalgesia were observed at the planter of hind paw innervated with involved L5 root in lumbar root constriction model, which means hypersensitive responses to both the mechanical stimulation transmitted with Aβ-fiber and the thermal stimulation transmitted with C-fiber. It is considered that neuropeptides such as NGF and BDNF are transported anterogradely in via spinal roots to DRG neuron to dorsal horn in spinal cord. These neuropeptides play an important role in central sensitization resulting in allodynia and hyperalgesia. In the current lumbar constriction model, the injury proximal to DRG blocks the transportation of the neuropeptide. Thus there may be different mechanism of mechanical allodynia and thermal hyperalgesia between the current root injury model and the peripheral injury model, that is to say, proximal and distal to DRG. The abundant TH-immunoreactive fibers in involved DRGs may be a plausible explanation for effectiveness of sympathetic block and suggest that the sympathetic nerve system may be related to a trigger of radicular pain.

REFERENCES: